

Self-management of COPD and its exacerbations

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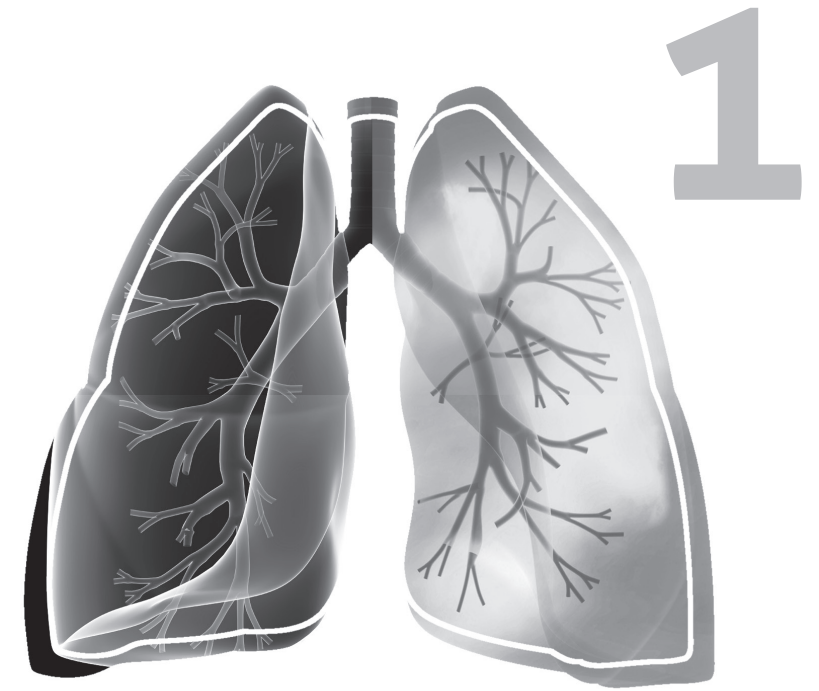
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Not the strongest species survives, nor the most intelligent, but the most adaptive.

Charles Darwin (1859)

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General introduction

Case history

Recently, I visited Mr S, a 67-year-old retired bank employee, after he had contacted my practice because of severe shortness of breath. Although Mr S had been listed with my practice for many years, I couldn't remember his face, as apparently, Mr S only seldomly consulted his general practitioner. His medical record showed that his wife had died almost 4 years ago. Upon more detailed examination of his record, I saw that Mr S had been diagnosed with COPD 5 years ago. At that time, his spirometry results showed a postbronchodilator FEV₁ of 53% percentage predicted. Surprisingly, he had never been prescribed any pulmonary medication, nor had he ever consulted the general practice in relation to his COPD after the initial diagnosis.

When I entered his apartment I was overwhelmed by a thick blue cloud of cigarette smoke. Mr S was sitting in his chair, bent forward, wheezing, with a lit cigarette. He had experienced shortness of breath for more than one week and was coughing up a lot of thick yellowish sputum. For the last two days he had not been able to leave his chair.

His dyspnoea did not improve with the bronchodilators I administered to him. I contacted a chest physician from the nearby hospital and asked him to evaluate Mr S at the emergency department. Mr S spent one week in the hospital and received oxygen, bronchodilators, prednisolon and antibiotics. It took him six weeks to recover completely and to return to his daily activities.

Introduction

The current prevalence of Chronic Obstructive Pulmonary Disease (COPD) casts a heavy burden on healthcare systems worldwide. People with COPD may suffer from mild to very severe symptoms, such as dyspnoea, cough, sputum, and fatigue. Obviously, these symptoms can have an immense impact on the daily functioning in every aspect and therefore quality of life. In addition, COPD is characterised by exacerbations, i.e. periods of sustained symptom worsening that may be very disabling and require medical attention.

Despite the current impact of COPD on patients and healthcare systems, there is still a high degree of undertreatment among patients with COPD regarding pharmacological and non-pharmacological management,¹ particularly in primary care.^{2,3} This is illustrated by the case history presented above. If the burden of COPD is to be relieved, new strategies to manage the disease are essential. In this context, COPD self-management interventions are promising. Briefly, self-management strategies comprise comprehensive chronic care tailored to individual needs and focused on the enhancement of patients' abilities to self-manage their disease proactively.

In this thesis, the importance and effects of self-management strategies for COPD and its exacerbations are described. Also, trends in the impact of COPD on primary care are examined, as well as the importance of adequate exacerbation measurement. This information helps to understand the role of self-management for COPD and its exacerbations in daily practice and clinical studies.

Defining COPD and its exacerbations

Chronic diseases are defined as conditions that are persistent and are usually characterised by slow progression. Chronic diseases can be controlled but not cured. According to the World Health Organisation (WHO), chronic conditions such as heart disease, diabetes, and chronic respiratory diseases are by far the leading cause of mortality in the world, accounting for 63% of all deaths.⁴ COPD represents the majority of chronic respiratory diseases. In 2004, COPD was the third leading cause of death in middle-income countries and the fifth leading cause of death in high-income countries,⁵ indicating that this disease is a major health problem in both developed and developing countries.

According to the Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD), COPD can be defined as "a common preventable and treatable disease that is characterised by a persistent and usually progressive airflow obstruction and an enhanced chronic inflammatory airway response."⁶ By far, tobacco smoking is

the most important risk factor for COPD. Indoor, outdoor and occupational air pollution are also associated with the development of COPD.⁷ As the definition of COPD is based on airflow limitation, lung function testing with a spirometer is essential in the process of diagnosing patients. However, patients do not actually suffer from the airflow limitation, but from symptoms and limitations in daily life which are only weakly correlated to the obstruction measured.⁸ COPD symptoms impact daily functioning, such as physical activity, and quality of life. As the disease progresses, symptoms gradually worsen and patients may become increasingly disabled.

In the progression of the disease many patients with COPD suffer from exacerbations. An exacerbation of COPD is an acute worsening of patient's respiratory symptoms that is beyond the normal day-to-day variation. Exacerbations significantly affect the patient's quality of life.^{9,10} It may take weeks before symptoms and lung function recover to baseline levels.¹¹ Exacerbations may accelerate the decline in lung function.¹² In turn, the worsening of airflow limitation increases the risk of exacerbations.¹³ Medical costs related to the treatment of exacerbations contribute considerably to the total costs attributed to COPD.¹⁴

Although the impact of COPD and its exacerbations on a patient's life is progressive, it may vary between and within patients. Consequently, there is a need for COPD management that is dynamic and continuously tailored to the individual patient's needs by considering the impact of all different aspects of the disease at any moment in his or her disease progress.

The impact of COPD and its exacerbations

To successfully introduce novel management strategies, the impact of COPD on the patient, as well as on the healthcare system should be taken into account. Estimates of the current burden of COPD are primarily based on mortality figures produced by registration systems of countries worldwide or prevalence estimates retrieved from population-based surveys.¹⁵ It should be realised that these estimates do not reflect the true impact of the disease on daily care.

Estimates of COPD prevalence and exacerbation occurrence rates obtained from daily practice may be a better indication of the disease impact. Although these measures do not reflect the burden on the individual patient, they do show how the COPD population affects daily care. Most patients with COPD are treated in general practice.¹⁶ It is estimated that male and female COPD patients represent 2.2% and 1.7% of all general practice patients respectively.¹⁷ Information on the occurrence rates of exacerbations in general practice is lacking. Two important reasons for this are: 1) there is still no consensus about the exact definition of an exacerbation¹⁸; and 2) current tools to detect exacerbations often lack validity testing or demonstrate

other limitations. For example, the validity of diary cards to record exacerbations is unknown and among study participants, there is low compliance for its use.¹⁹ Despite this, diary cards are still the most frequently used method to record exacerbations. There is therefore a need for valid instruments with high compliance that can detect the various definitions of exacerbations to gain more information on exacerbation occurrence rates.

To put the current burden of COPD in general practice into the right perspective, information on past trends in COPD prevalence and exacerbation occurrence rates is essential. Yet, little is known about how COPD prevalence or COPD exacerbation rates have changed over time in daily practice.

COPD disease management

As with other chronic conditions, COPD cannot be cured. Management of patients with COPD focuses on the stabilization of disease progression and the decrease of symptoms and limitations (see box 1).²⁰ For a long time, a certain nihilism in COPD management has existed among healthcare professionals and patients, however this has changed in the last decade due to the development of new medication and new insights in the importance of life-style factors, such as physical activity. But still, as stated earlier, COPD is a grossly undertreated condition. Raising the awareness of COPD as a major health problem among professionals and patients and reorganising the management of COPD may help to alter this.

In the Netherlands, the recent reform of general practice organisation and the introduction of innovations in chronic care²¹ may answer the call for a renewed focus on COPD disease management. One of the innovations was the introduction

Box 1 Goals of effective COPD management according to the WHO

- Prevent disease progression
- Relieve symptoms
- Improve exercise tolerance
- Improve health status
- Prevent and treat complications
- Prevent and treat exacerbations
- Reduce mortality

Source: adapted from reference 20.

of the practice nurse in 1999, which led to the delegation of many tasks concerning chronic care from GPs to nurses and the development of structured care programmes including regular reviews. Although this did not result in a marked decrease in the GPs' workload, it did benefit the quality of care for patients with chronic conditions²² and resulted in higher patient satisfaction in relation to the time available to the patient and support.²³ For COPD, the evidence base for regular practice nurse-based reviews is missing so far.²⁴ At the same time, the majority of Dutch general practices are implementing structured practice nurse-coordinated COPD management programmes. The programmes follow current COPD guidelines provided by professional organisations, such as the Dutch College of General Practitioners (*Nederlands Huisartsen Genootschap* [NHG])²⁵ and the Dutch Lung Alliance (*Long Alliantie Nederland* [LAN]).²⁶ The most recent guidelines advocate the implementation of self-management strategies as part of structured COPD management.^{26,27} Self-management strategies perfectly suit the concept of collaborative care in which the patient actively participates in the decision making of disease management.²⁸ Table 1 describes the differences between traditional and collaborative care in chronic illness. It should be noted that in this context collaborative care is compared to the 'traditional' structured protocolized care of regular reviews. From the perspective of the healthcare system, implementing self-management strategies may have the potential to decrease the COPD burden by promoting proactive disease management by the patients themselves.

COPD self-management

Patients with COPD are confronted with their disease every day and are forced to make day-to-day decisions about how to cope with symptoms and limitations. Patients who do not (yet) experience any disabilities also make decisions that may influence their disease, e.g. they decide whether or not to quit smoking, start physical activity, or lose weight. Obviously, there is already a certain level of self-management in patients with COPD. However, patients may make wrong decisions (as pictured in the case history) due to insufficient disease knowledge or inadequate self-management skills. COPD self-management programmes refer to interventions that aim to teach patients the skills needed to carry out medical regimens specific for a long-term disease and to guide behaviour change to help patients control their own condition and improve their well-being.²⁹ Presently, the number of COPD self-management programmes is growing which results in varying definitions and contents.³⁰ This explains why meta-analyses on the effects of COPD self-management have failed to show compelling results so far.³¹ Obviously, researchers and professionals have to adopt a common position on the process and practice of

Table 1 Traditional care *versus* collaborative care in chronic illness

Issue	Traditional care	Collaborative care
Relationship between patient and health professional	Professional is the expert who tells the patient what to do. Patient is passive.	Shared expertise: the patient is expert about his/her body, the professional is expert about the disease. The patient is active.
Principal caregiver and responsible party for outcomes	The professional.	Both patient and professional: they share responsibility for solving problems and for outcomes.
Goal	Compliance with instructions. Non-compliance is a personal deficit of the patient.	Patient sets goals, professional assists to make informed choices. Inability to achieve goals requires modification of strategies.
Changing behaviour	By external motivation.	By internal motivation. Patient gains understanding and confidence to adapt behaviour.
Identifying problems	By the professional, e.g. changing unhealthy behaviour.	By the patient, e.g. limitation in daily functioning; and by the professional.
Solving problems	Professional solves problems for patient.	Professional teaches problem-solving skills and supports patient in solving problems.

Source: adapted from reference 28.

COPD self-management. Yet, the evidence base of COPD self-management programmes is steadily growing, particularly in secondary care.^{29;32} In primary care - where self-management strategies may be needed the most - the effects remain inconclusive.

Despite the enormous impact exacerbations may have, many patients fail to recognise an exacerbation.³³ Also, patients may fail to respond timely in the course of symptom worsening, thereby increasing the risk of complications such as hospital admission.³⁴ Consequently, exacerbation management aimed at early recognition and prompt treatment of exacerbations deserve a prominent place in COPD disease management. The use of a written exacerbation action plan, often embedded in a comprehensive COPD self-management programme, seems to aid the recognition of, and promote prompt action in response to severe exacerbations.^{35;36} However, the effect of a written exacerbation action plan on exacerbation-related issues, such as symptom recovery or the risk of complications, remains unclear. Therefore, the implementation of action plans in daily practice cannot yet be persuasively recommended.³⁵

Objectives of this thesis

Based on the needs arising from daily practice and the flaws observed in research on the impact of COPD and self-management of COPD and its exacerbations as discussed above, this thesis addresses the following objectives:

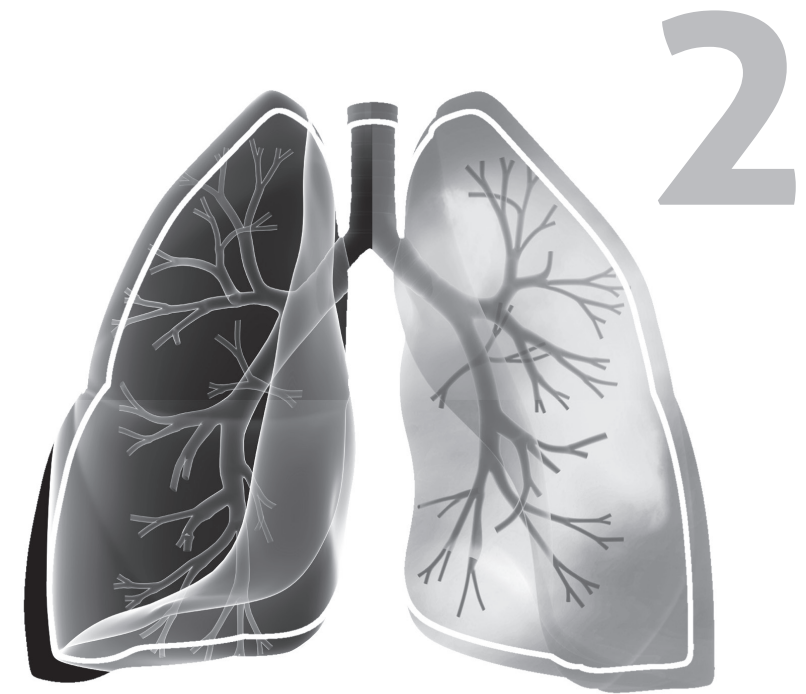
1. To describe long-term trends in COPD prevalence and exacerbation occurrence rates in Dutch general practice.
2. To assess the validity of an automated telephonic exacerbation assessment system to record exacerbation rates in prospective clinical studies and to relate its results to other exacerbation detection tools.
3. To describe the concept and practice of self-management and its potential role in the prevention and early treatment of COPD exacerbations.
4. To assess the long-term effects on quality of life of two different modes of COPD disease management in general practice i.e. comprehensive self-management and routine monitoring.
5. To assess the effects of a written action plan for COPD exacerbations on exacerbation recovery time and unscheduled healthcare utilisation.

Outline of this thesis

In *Chapter 2*, the impact of COPD in the Dutch general practice is depicted by the results of a trend study on the prevalence of COPD and its exacerbations using long-term data of a prospective, dynamic, general practice-based cohort. In *Chapter 3*, the results of a Canadian trend study on COPD prevalence are reviewed in the context of the results described in *Chapter 2*. The validity of the Nijmegen telephonic exacerbation assessment system (TEXAS) and its results relative to other exacerbation detection tools are presented in *Chapter 4*. In *Chapter 5*, the concept and practice of COPD self-management is described with a specific focus on prevention and early treatment of COPD exacerbations. *Chapter 6* presents the effect on quality of life of comprehensive COPD self-management and routine monitoring of patients with COPD in the general practice. The effects of a written COPD exacerbation action plan on exacerbation recovery time and unscheduled healthcare utilisation are described in *Chapter 7*. Finally in *Chapter 8*, the preceding chapters are summarised and discussed in the light of previous research and future perspectives.

References

1. Make B, Dutro MP, Paulose-Ram R, Marton JP, Mapel DW. Undertreatment of COPD: a retrospective analysis of US managed care and Medicare patients. *Int J Chron Obstruct Pulmon Dis* 2012;7:1-9.
2. Bourbeau J, Sebaldt RJ, Day A, Bouchard J, Kaplan A, Hernandez P et al. Practice patterns in the management of chronic obstructive pulmonary disease in primary practice: The CAGE study. *Can Respir J* 2008;15:13-19.
3. Takahashi T, Ichinose M, Inoue H, Shirato K, Hattori T, Takishima T. Underdiagnosis and undertreatment of COPD in primary care settings. *Respirology* 2003;8:504-8.
4. Global status report on non-communicable diseases 2010. Geneva: World Health Organization: Available from URL: http://www.who.int/nmh/publications/ncd_report2010/en/index.html; Date last accessed: May 2012.
5. The global burden of disease: 2004 update. Geneva: World Health Organization: Available from URL: http://www.who.int/healthinfo/global_burden_disease/2004_report_update/en/index.html. Date last updated: June 2011; date last accessed May 2012.
6. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease. Revised 2011. Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD): Available from URL: <http://www.goldcopd.org>. Date last updated: December 2011; Date last accessed: May 2012.
7. Salvi S, Barnes P. Chronic obstructive pulmonary disease in non-smokers. *Lancet* 2009;374:733-43.
8. Jones P. Health status and the spiral of decline. *COPD* 2009;59-63.
9. Langsetmo L, Platt RW, Ernst P, Bourbeau J. Under-reporting Exacerbation of COPD in Longitudinal Cohort. *Am J Respir Crit Care Med* 2008;177:396-401.
10. Seemungal TA, Donaldson GC, Paul EA, Bestall JC, Jeffries DJ, Wedzicha JA. Effect of exacerbation on quality of life in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1998;157:1418-22.
11. Seemungal TA, Donaldson GC, Bhowmik A, Jeffries DJ, Wedzicha JA. Time course and recovery of exacerbations in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2000;161:1608-13.
12. Donaldson GC, Seemungal TA, Bhowmik A, Wedzicha JA. Relationship between exacerbation frequency and lung function decline in chronic obstructive pulmonary disease. *Thorax* 2002;57:847-52.
13. Hoogendoorn M, Feenstra T, Hoogenveen R, Al M, Mölken M. Association between lung function and exacerbation frequency in patients with COPD. *Int J Chron Obstruct Pulmon Dis* 2010;435-44.
14. Wedzicha J, Seemungal T. COPD exacerbations: defining their cause and prevention. *Lancet* 2007;370:786-96.
15. Lopez AD, Shibuya K, Rao C, Mathers CD, Hansell AL, Held LS et al. Chronic obstructive pulmonary disease: current burden and future projections. *Eur Respir J* 2006;27:397-412.
16. Bellamy D, Bouchard J, Henrichsen S, Johansson G, Langhammer A, Reid J et al. International Primary Care Respiratory Group (IPCRG) guidelines: management of chronic obstructive pulmonary disease (COPD). *Prim Care Respir J* 2006;15:48-57.
17. Boezen HM, Postma DS, Smit HA, Poos MJ. Hoe vaak komt COPD voor en hoeveel mensen sterven eraan? Volksgezondheid Toekomst Verkenning, Nationaal Kompas Volksgezondheid 2010. Bilthoven: RIVM: Available from URL: <http://www.nationaalkompas.nl/gezondheid-en-ziekte/ziekten-en-aandoeningen/ademhalingswegen/copd/omvang/>. Date last accessed: May 2012.
18. Effing TW, Kerstjens HA, Monnickhof EM, Van der Valk PD, Wouters EF, Postma DS et al. Definitions of Exacerbations. Does It Really Matter in Clinical Trials on COPD? *Chest* 2009;136:923.
19. Stone AA, Shiffman S, Schwartz JE, Broderick JE, Hufford MR. Patient compliance with paper and electronic diaries. *Control Clin Trials* 2003;24:182-99.
20. Chronic respiratory diseases: COPD management. Geneva: World Health Organization. Available from URL: <http://www.who.int/respiratory/copd/management/en/index.html>. Date last accessed: April 2012.
21. van Weel C, Schers H, Timmermans A. Health care in the Netherlands. *J Am Board Fam Med* 2012;Suppl 1:S12-S17.
22. Laurant M, Harmsen M, Wollersheim H, Grol R, Faber M, Sibbald B. The impact of nonphysician clinicians: do they improve the quality and cost-effectiveness of health care services? *Med Care Res Rev* 2009;66:36S-89S.
23. Laurant MG, Hermens RP, Braspenning JC, Akkermans RP, Sibbald B, Grol RP. An overview of patients' preference for, and satisfaction with, care provided by general practitioners and nurse practitioners. *J Clin Nurs* 2008;17:2690-2698.
24. van den Bemt L, Schermer T, Smeele I, Bischoff E, Jacobs A, Grol R et al. Monitoring of patients with COPD: a review of current guidelines' recommendations. *Respir Med* 2008;102:633-41.
25. Smeele IJ, van Weel C, van Schayck CP, van der Molen T, Thoonen B, Schermer T. NHG-Standaard COPD. *Huisarts Wet* 2007;50:362-79.
26. Zorgstandaard COPD. Amersfoort: Long Alliantie Nederland (LAN). Available from URL: <http://www.longalliantie.nl/zorgstandaard-copd>. Date last accessed: May 2012.
27. Chronic obstructive pulmonary disease: Management of chronic obstructive pulmonary disease in adults in primary and secondary care. London: National Institute for Clinical Excellence (NICE) 2010. Available from URL: <http://publications.nice.org.uk/chronic-obstructive-pulmonary-disease-cg101>. Date last accessed May 2012.
28. Bodenheimer T, Lorig K, Holman H, Grumbach K. Patient self-management of chronic disease in primary care. *JAMA* 2002;288:2469-75.
29. Bourbeau J, Julien M, Maltais F, Rouleau M, Beaupre A, Begin R et al. Reduction of Hospital Utilization in Patients With Chronic Obstructive Pulmonary Disease: A Disease-Specific Self-management Intervention. *Arch Intern Med* 2003;163:585-91.
30. Effing T, Bourbeau J, Vercoulen J, Apter AJ, Coultas D, Meek P et al. Self-management programmes for COPD: moving forward. *Chron Respir Dis* 2012;9:27-35.
31. Effing T, Monnickhof EM, Van der Valk PD, van der Palen J, van Herwaarden CL, Partridge MR et al. Self-management education for patients with chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2007;4:CD002990.
32. Rice K, Dewan N, Bloomfield H, Grill J, Schult T, Nelson D et al. Disease Management Program for Chronic Obstructive Pulmonary Disease. A Randomized Controlled Trial. *Am J Respir Crit Care Med* 2010;182:890-896.
33. Kessler R, Stahl E, Vogelmeier C, Haughney J, Trudeau E, Lofdahl CG et al. Patient understanding, detection, and experience of COPD exacerbations: an observational, interview-based study. *Chest* 2006;130:133-42.
34. Wilkinson TM, Donaldson GC, Hurst JR, Seemungal TA, Wedzicha JA. Early therapy improves outcomes of exacerbations of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2004;169:1298-303.
35. Walters J, Turnock A, Walters E, Wood-Baker R. Action plans with limited patient education only for exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2010;May 12;(5):CD005074.
36. Sedeno M, Nault D, Hamd D, Bourbeau J. A self-management education program including an action plan for acute COPD exacerbations. *COPD* 2009;6:352-58.



Trends in COPD prevalence and exacerbation rates in Dutch primary care

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Abstract

Background

Changes in the burden of chronic obstructive pulmonary disease (COPD) and its exacerbations on primary health care are not well studied.

Aim

To identify trends in the prevalence of physician-diagnosed COPD and exacerbation rates by age, sex, and socioeconomic status in a general practice population.

Design of study

Trend analysis of COPD data from a 27-year prospective cohort of a dynamic general practice population.

Setting

Data were taken from the Continuous Morbidity Registration Nijmegen.

Method

For the period 1980–2006, COPD and COPD exacerbation data were extracted for patients aged ≥ 40 years. Data were standardised for the composition of the Continuous Morbidity Registration population in the year 2000. Regression coefficients for trends were estimated by sex, age, and socioeconomic status. Rate ratios were calculated for prevalence differences in different demographic subgroups.

Results

During the study period, the overall COPD prevalence decreased from 72.7 to 54.5 per 1000 patients per year. The exacerbation rate decreased from 44.1 to 31.5 per 100 patients, and the percentage of patients with COPD who had exacerbations declined from 27.6% to 21.0%. The prevalence of COPD increased significantly in women, in particular those aged ≥ 65 years with low socioeconomic status. Decreases in exacerbation rates and percentages of patients with exacerbations were independent of sex, age, and socioeconomic status.

Conclusion

The decline in COPD prevalence and exacerbation rates suggests a reduction of the burden on Dutch primary care. The increase of the prevalence in women indicates a need to focus on this particular subgroup in COPD management and research.

Introduction

The prevalence of chronic obstructive pulmonary disease (COPD) and its subsequent burden on health care differ from country to country but is extensive in most populations.¹ COPD exacerbations contribute substantially to the burden by generating the majority of costs due to the use of healthcare services² and by provoking significant impact on patients' health status.³ In the Netherlands, the burden of COPD mainly affects GPs as most patients with COPD are managed in primary care; as such, there is a growing need to identify changes in the burden and to redirect care to those demographic subgroups that are at highest risk of COPD and its exacerbations. In this context, trend studies may be very useful. So far, most COPD trend studies have used data from national health surveys to estimate trends in the general population,^{4,5} and so their results may not reflect the burden in general practice.

A recent trend study using data from a general practice network demonstrated a constant rise of physician-diagnosed COPD in women.⁶ This could be caused by the increase of tobacco use in women relative to men in the past few decades. The risk of developing COPD in smokers is related to the lifetime cumulative dose, which explains the finding that it is mostly diagnosed in people aged ≥ 65 years and is highly unlikely in those aged < 40 years.⁵ Independent from smoking, socioeconomic status is an important risk factor for COPD.⁷ In addition, factors linked to socioeconomic status, such as respiratory tract infections, housing conditions, air pollution, and diet each contribute to the risk of having exacerbations.^{8–10} Obviously, sex, age, and socioeconomic differences are important factors that can influence trend changes of COPD and exacerbations. Although these factors are well registered in general practice registration networks, their roles have not been well studied in COPD trend studies in primary care.

In this article, long-term trends in physician-diagnosed COPD prevalence and COPD exacerbations in the period 1980–2006 are reported by prospectively studying a dynamic cohort from the Continuous Morbidity Registration Nijmegen. The aim was to identify trend changes in COPD prevalences and COPD exacerbation occurrence rates in different subgroups of the general practice population.

Method

Setting

The Continuous Morbidity Registration of the Department of Primary and Community Care of the Radboud University Nijmegen Medical Centre is a prospective cohort study in which four Dutch general practices with a registered practice population of approximately 15 000 subjects in the Nijmegen area have participated since 1967. It is

a relatively stable practice population that reflects the Dutch healthcare system, that is, all patients are registered with a GP and all access to care is through referral by the GP.¹¹ Since its founding, the Continuous Morbidity Registration Nijmegen has served as a successful practice-based research network for many primary care studies.¹²

The GPs of the Continuous Morbidity Registration practices record all diagnoses of all new episodes of illness in a standardised way, based on the E-list that is used to register morbidities in general practice¹³ and the International Classification of Health Problems in Primary Care.¹⁴ Recurrence of an episode after successful treatment or natural recovery (that is, a patient reporting that respiratory symptom aggravation recurred after a period in which exacerbation symptoms had returned to baseline level) is considered as a new episode. Chronic conditions such as COPD are coded annually after the year of initial diagnoses.¹⁵ Diagnoses made by specialists after referral are reported back to the GP and are entered in the database. The validity of the recorded diagnoses in the Continuous Morbidity Registration has been shown to be well above 80% in a variety of conditions.^{16,17}

Subjects and definition of variables

Patients diagnosed with COPD were identified for the period 1980–2006 and were included in the annual prevalence rates from the first year of diagnosis. All patients were retrieved from the database with the E-list codes 'chronic bronchitis', 'lung emphysema', and 'COPD'. In the Continuous Morbidity Registration, COPD exacerbation was defined as an acute episode of respiratory symptom worsening, for which the patient, registered with a diagnostic code compatible with COPD, consulted the GP. Diagnosed exacerbations were recorded separately by adding a unique code for exacerbations to the diagnostic code for COPD or by using the E-list code 'acute bronchitis' or 'chronic bronchitis' in patients previously diagnosed with COPD. Exacerbation follow-up contacts were not considered as new events.

A small and, in time, significantly decreasing proportion of patients aged <40 years was observed in the Continuous Morbidity Registration. Given this small proportion and the opinion that COPD is highly unlikely in subjects aged <40 years, trend analyses were limited to data from patients with COPD who were aged ≥40 years. Age was grouped into two bands: 40–64 years and ≥65 years. Socioeconomic status was determined by classifying the occupation of the patient using the Netherlands Standard Classification of Occupations 1992.¹⁸ The coded occupations were ranked into low, medium, and high socioeconomic status. Due to very low prevalence rates and small group sizes in the high socioeconomic status group, the medium and high socioeconomic status groups were joined in the trend analyses and will be presented as 'medium to high socioeconomic status'.

Statistical analyses

The number of patients with COPD and the frequency of exacerbations per patient were counted annually. Prevalence and exacerbation rates were standardised for the composition of the Continuous Morbidity Registration population in the year 2000 by age, sex, and socioeconomic status. Univariate regression analyses were conducted on the annual COPD prevalences and exacerbation rates using SPSS (version 16.0.2., SPSS Inc, Chicago). Regression coefficients for trends (RC trends) should be interpreted as the annual change in prevalence per 1000 patients per year. An RC trend was considered statistically significant if the 95% confidence interval (CI) did not include 0 and if $P < 0.05$.

Rate ratios (RRs) were calculated by dividing the annual prevalence or occurrence rate of two different subgroups (that is, males versus females, medium to high socioeconomic status versus low socioeconomic status, 40–64 years versus ≥65 years).

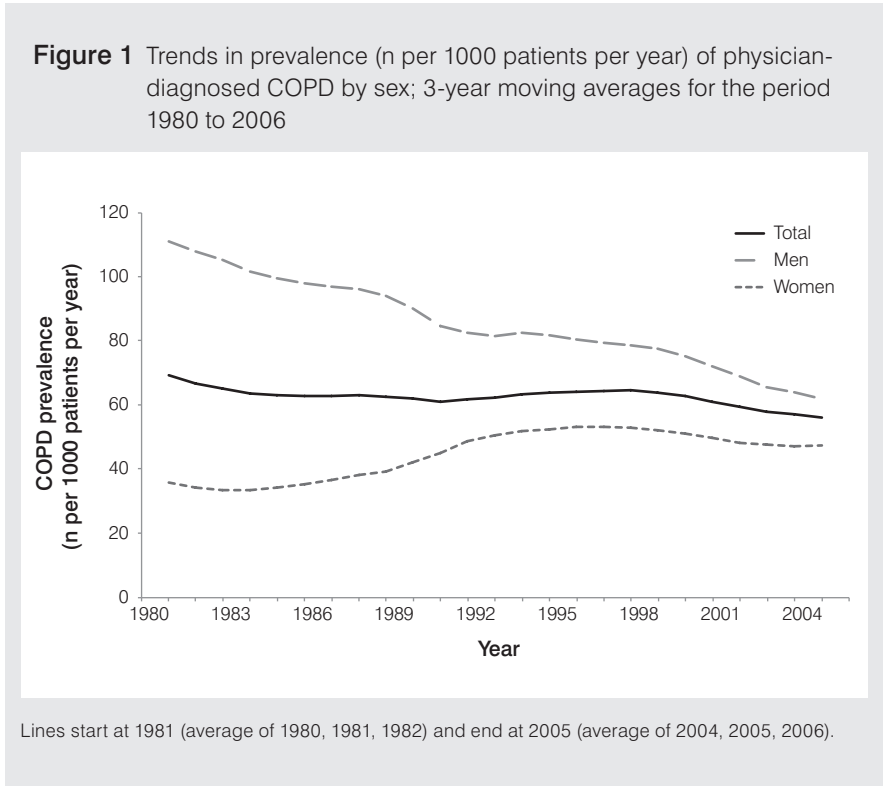
In the exacerbation data an apparent split was observed in 1986 that may have been caused by a change in the registration of exacerbations; therefore, regression analyses were conducted on exacerbation data from 1986 onwards. Figures 2 and 3 presenting exacerbation rates also show data from 1980 to 1985.

Prevalence rates are presented as the number of COPD cases per 1000 patients per year and exacerbation rates as the number of exacerbations per 100 patients with COPD per year.¹⁵ The presented Figures 1–3 show 3-year moving average rates to reduce the effect of random variation in consecutive calendar years.

Results

Trends in COPD

In 1980, a total of 423 patients aged ≥40 years with physician-diagnosed COPD could be detected in the Continuous Morbidity Registration population. The prevalence per 1000 patients per year was 72.7. In 2006, the number of patients with COPD had decreased to 317 with a prevalence of 54.4 patients per 1000 patients per year. Figure 1 shows trends in COPD prevalence for the total cohort and for men and women separately. In 1980, COPD prevalence in men was higher than in women (RR = 3.1), but decreased from 115.2 patients per 1000 patients per year to 59.0 patients per 1000 patients per year (RC trend = -1.92 , 95% CI = -2.06 to -1.77) in 2006. In contrast, the COPD prevalence in women increased from 37.5 patients per 1000 patients per year in 1980 to 47.2 patients per 1000 patients per year in 2006 (RC trend = 0.73 , 95% CI = 0.49 to 0.96), thereby closing the gender gap (RR = 1.2). Table 1 presents prevalence estimates by sex combined with age and socioeconomic status.



In men and women the prevalence rates were highest in patients aged ≥ 65 years with a low socioeconomic status. The strongest increase in COPD prevalence was observed in women of low socioeconomic status aged ≥ 65 years (prevalence difference 1980–2006 = 46.5 per 1000 patients per year, RC trend = 2.55, 95% CI = 2.02 to 3.09), while the strongest decrease in COPD prevalence was demonstrated in men of low socioeconomic status aged ≥ 65 years (prevalence difference 1980–2006 = –134.1 per 1000 patients per year, RC trend = –5.17, 95% CI = –6.23 to –4.12). In all male subgroups the COPD prevalence trends showed a statistically significant decrease in the regression analyses.

Trends in COPD exacerbations

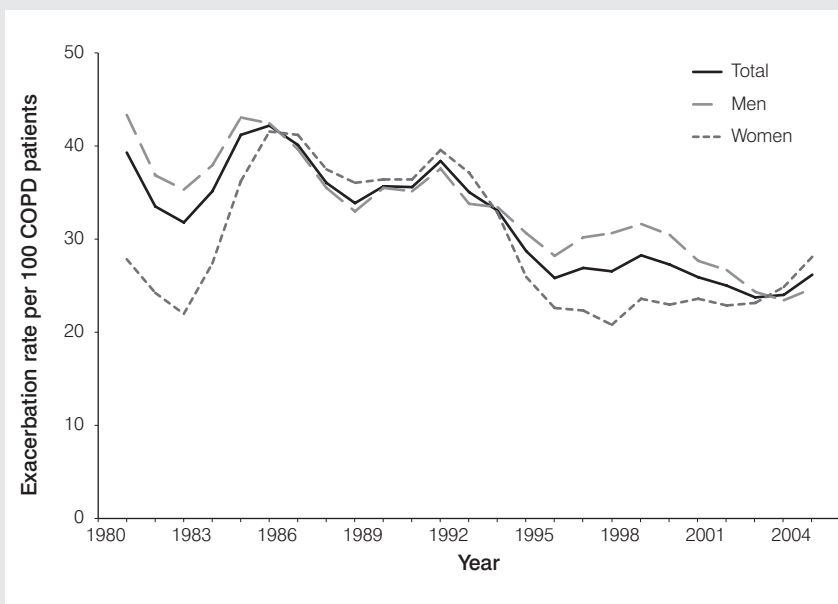
From 1980 until 2006, a total of 2831 exacerbations were recorded by the GPs in the Continuous Morbidity Registration practices. Figure 2 presents trend curves for the annual exacerbation rates in the total COPD population and in men and women separately. The trend curve in the total COPD cohort showed a gradual decline from 1986 onwards, from 45.2 to 31.5 exacerbations per 100 patients with COPD.

Table 1 Prevalence rates of physician-diagnosed COPD by sex, age and socioeconomic status for the period 1980 to 2006

Population subgroup	Prevalence per 1000 patients per year		Prevalence differences between 1980-2006 (%)	Regression Coefficient trend (95% CI) #	P-value for trend
	1980	2006			
Men					
Aged 40 to 64 years with low socioeconomic status	76.3	42.0	- 34.3 (44.9%)	-0.98 (-1.24 to -0.71)	< 0.001
Aged 40 to 64 years with medium to high socioeconomic status	56.4	16.3	- 40.1 (71.0%)	-1.30 (-1.56 to -1.04)	< 0.001
Aged ≥ 65 years with low socioeconomic status	311.5	177.4	- 134.1 (43.0%)	-5.17 (-6.23 to -4.12)	< 0.001
Aged ≥ 65 years with medium to high socioeconomic status	216.7	154.3	- 62.4 (28.8%)	-1.55 (-2.04 to -1.05)	< 0.001
Women					
Aged 40 to 64 years with low socioeconomic status	26.2	38.9	12.7 (48.7%)	0.61 (0.44 to 0.79)	< 0.001
Aged 40 to 64 years with medium to high socioeconomic status	17.1	13.2	- 3.9 (23.2%)	-0.033 (-0.20 to 0.13)	0.68
Aged ≥ 65 years with low socioeconomic status	88.8	135.3	46.5 (52.4%)	2.55 (2.02 to 3.09)	< 0.001
Aged ≥ 65 years with medium to high socioeconomic status	58.7	88.5	29.8 (50.7%)	2.25 (1.85 to 2.65)	< 0.001

The regression coefficient trend reflects the annual change in prevalence per 1000 patients per year.

Figure 2 Trends in exacerbation rates (n per 100 patients per year) of patients with physician-diagnosed COPD; 3-year moving averages for the period 1980 to 2006. Trends were analysed for the period 1986–2006.

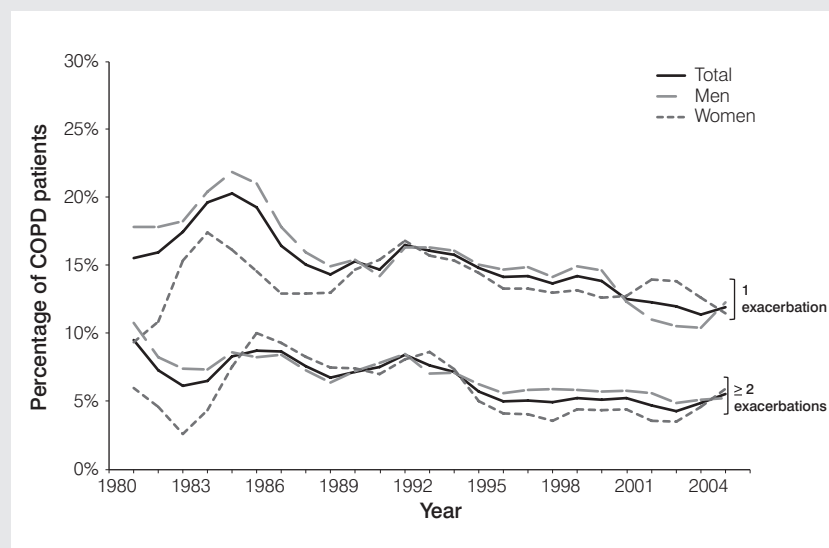


Lines start at 1981 (average of 1980, 1981, 1982) and end at 2005 (average of 2004, 2005, 2006).

The estimated trend regression coefficient showed a decrease of 0.82 exacerbations per 100 COPD patients per year (95% CI = -1.14 to -0.50). This trend was also observed in men (RC trend = -0.77 , 95% CI = -1.09 to -0.45) and women (RC trend = -0.94 ; 95% CI = -1.41 to -0.46) when analysed separately. The rate ratio for men versus women varied from 0.92 in 1986 to 1.26 in 1996 and 0.80 in 2006. The separate trend curves for patients aged 40–64 years and ≥ 65 years and for patients of low socioeconomic status and medium to high socioeconomic status also showed a statistically significant decline. After combining sex with age and socioeconomic status, the number of exacerbations became too small to estimate trend regression coefficients.

Figure 3 shows trends in patients with COPD who have exacerbations for the total COPD cohort and for men and women separately. In 1986, 20.4% of patients with COPD reported one exacerbation and 9.2% reported two or more exacerbations.

Figure 3 Trends in COPD patients with exacerbations (% of total COPD patients): 3-year moving averages for the period 1980–2006. Trends were analysed for the period 1986–2006.



Lines start at 1981 (average of 1980, 1981, 1982) and end at 2005 (average of 2004, 2005, 2006).

In 2006, the percentage of patients with exacerbations had decreased to 14.6% for patients with one exacerbation (RC trend = -0.26 , 95% CI = -0.42 to -0.11) and to 6.4% for patients with two or more exacerbations (RC trend = -0.19 , 95% CI = -0.29 to -0.093). The separate trend curves for male and female patients with COPD who have exacerbations also showed a significant decrease. The trend curves by age and socioeconomic status were comparable to the trend curves by sex. Again, the number of patients having exacerbations became too small to conduct further analyses when combining sex with age and socioeconomic status.

Discussion

Summary of main findings

Using data from the Continuous Morbidity Registration Nijmegen, this study demonstrated that the overall prevalence of physician-diagnosed COPD has decreased significantly during the last decades. The annual rates of exacerbations

and proportions of patients with COPD who had exacerbations had also decreased. These findings suggest a reduction rather than an increase of the COPD burden on Dutch primary care.

When analysing prevalence trends by sex, age, and socioeconomic status a significant increase of COPD prevalence in women was observed, in particular in those aged ≥ 65 years of low socioeconomic status. In men, on the other hand, the prevalence of COPD had decreased, independent of age and socioeconomic status. The decreasing trend curves for exacerbation rates and percentage of patients with exacerbations were independent of sex, age, and socioeconomic status.

Strengths and limitations of the study

The strengths of the current study are the long follow-up period and the standardised way of recording COPD and COPD exacerbations in all four general practices. The decision to present prevalence rates from the period 1980 and onwards was mainly based on the validity of the data prior to 1980. As three of the four practices started with morbidity registration in 1967 and the fourth practice joined the registration network in 1971, the first years after 1967 were considered as a 'run-in-period'. When studying all COPD data in the Continuous Morbidity Registration, very low prevalence rates were found in the first years of registration followed by a sharp increase in the following years. This 'run-in period' has been confirmed by the oldest generation among the current GPs in the four practices. By choosing 1980 as a starting point there was greater confidence about the validity of the data; having 2006 as the end date meant it was possible to cover a very long and unique timeframe. In addition, the information in the Continuous Morbidity Registration may be considered as complete because diagnoses made by specialists are reported back to the GP and are also entered in the database. This makes the Continuous Morbidity Registration a unique database for long-term trend analyses. However, as this study had an observational design, it cannot prove causality and, as such, the results should be interpreted with care.

Although the population of the Continuous Morbidity Registration reflects the Dutch general population regarding sex and age,¹² the network consists of only four practices. This may have caused the limited annual number of recorded exacerbations when analysing the different subgroups of male and female patients. Although it seems reasonable to assume that changes in smoking patterns will have attributed to the changes in prevalence and exacerbations trends, there is a lack of valid information regarding smoking status in the Continuous Morbidity Registration. This is not unique for this registration network, but is a concern to all general practice research networks that rarely use uniform definitions to document current or past smoking habits.¹⁹

Since 1996, diagnosing COPD in the Continuous Morbidity Registration practices has changed from a physician-based diagnosis to a more objective diagnosis using lung-function measurements according to COPD guidelines.^{20,21} This could have provoked a change in the overall prevalence of physician-diagnosed COPD, but this was not observed in prevalence trends from 1996 onwards.

Comparison with existing literature

Accurately estimating the prevalence of COPD very much depends on the study population and the study methods.²² Therefore, the prevalence rates in the current study should be compared with other prevalence rates based on physician-reported diagnoses. Although a higher prevalence rate was found than the UK trend study published in 2000,⁶ the finding is in line with a recent study that showed a pooled prevalence of 5.2% (95% CI = 3.3% to 7.9%).²³

The gradual decline in the prevalence of COPD between 1980 and 2006 seems to be mainly caused by the sharp decrease of the prevalence in men, independent of age and socioeconomic status. The rise of COPD prevalence in women has been reported previously.^{5,6} However, the current study is the first to actually demonstrate that the strongest increase is in women aged ≥ 65 years of low socioeconomic status. This finding is likely to reflect the increase of tobacco use in this subgroup during the last decades. Between 1960 and 1981, smoking rates have decreased sharply in Dutch men and recently smoking rates have also started to decrease in women, in particular those aged 20–34 years.²⁵ If this decline continues, the increasing prevalence of COPD in women is likely to have its peak in the next decades.

It could be questioned whether the current results reflect the true burden of the disease in primary care as GPs tend to under-diagnose COPD^{26,27} and patients may fail to present their symptoms.²⁸ A third of current smokers in general practice has undiagnosed COPD²⁹ although a substantial proportion shows respiratory symptoms that need treatment.²⁶ This implies that the true burden of COPD in primary care is far more extensive than would be expected when based on the results of the current study.

So far, there are no studies that show trends in exacerbation rates in patients in primary care. With overall annual exacerbations rates between 44.1 (1980) and 31.5 exacerbations (2006) per 100 patients with COPD, the mean exacerbation rate per patient was less than one reported exacerbation per 2 years in the current study. In addition, less than 30% of patients with COPD contributed to the total annual exacerbation rate and less than 10% could be considered as frequent exacerbators, that is, patients with COPD who have two or more exacerbations.²⁰ However, previous studies demonstrated that many patients have problems in recognising symptom aggravation³⁰ and fail to report the exacerbation to their health

professional.³¹ Although there is a relationship between age and the risk of underreporting,³² no difference was found in reported exacerbations between patients aged 40–64 years and patients aged ≥ 65 years. Also, there was no confirmation of the relationship between low socioeconomic status and the risk for exacerbations reported from secondary-care studies.^{8–10}

Although there is no straightforward explanation for the declining exacerbation trends, two different developments may have contributed to these findings. Vaccines and several pharmacological treatments (such as long-acting bronchodilators and inhaled corticosteroids) that may reduce exacerbation frequency and severity have been introduced in the last two decades;⁸ in addition, in 1992 the Dutch College of General Practitioners (NHG) introduced the first guideline on COPD management with a specific focus on the treatment of acute exacerbations.³³ This may have caused a change in the attitude of Dutch GPs towards the prevention and treatment of exacerbations.

Implications for future research and clinical practice

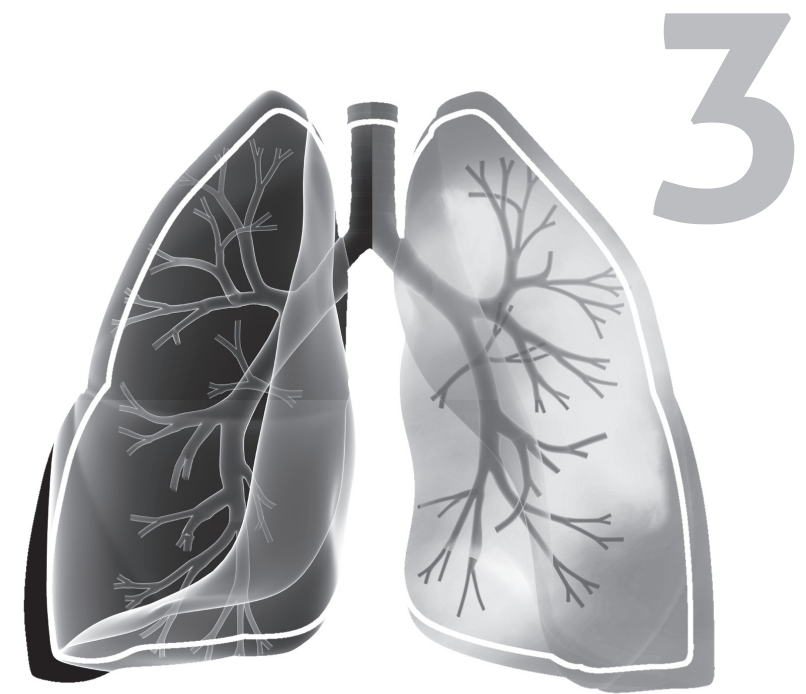
This study demonstrated that the prevalence of physician-diagnosed COPD has decreased in recent decades. Although this study did not investigate the prevalence of undiagnosed COPD in the practice population, GPs should be aware that many patients are still undiagnosed. The finding that the increasing prevalence of COPD in women is particularly noted in those aged ≥ 65 years with a low socioeconomic status indicates the need to focus more on this subgroup in COPD diagnosing, management, and research. The decrease in the number of recorded exacerbations and the decrease in the percentage of patients with COPD who have exacerbations are encouraging. However, as previously stated, the underreporting of worsening symptoms is a major concern in the management of patients with COPD. Improving patient understanding of the nature of an exacerbation and early recognition of its symptoms could benefit its reporting.

In conclusion, this is the first study that reports on long-term trends in COPD prevalence and exacerbation rates in primary care using unique registration data from the Continuous Morbidity Registration Nijmegen. The results from this study give more insight into trend changes in different demographic subgroups and may help GPs to redirect care and to diminish the burden of COPD.

References

1. Wouters EF. Economic analysis of the Confronting COPD survey: an overview of results. *Respir Med* 2003; 97 Suppl C: S3–14.
2. Sullivan SD, Ramsey SD, Lee TA. The economic burden of COPD. *Chest* 2000; 117(2 Suppl): 5S–9S.
3. Seemungal TA, Donaldson GC, Paul EA, et al. Effect of exacerbation on quality of life in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1998; 157: 1418–22.
4. Lacasse Y, Brooks D, Goldstein RS. Trends in the epidemiology of COPD in Canada, 1980 to 1995. COPD and Rehabilitation Committee of the Canadian Thoracic Society. *Chest* 1999; 116(2):306–313.
5. Mannino DM, Homa DM, Akinbami LJ, et al. Chronic obstructive pulmonary disease surveillance—United States, 1971–2000. *MMWR Surveill Summ* 2002; 51(6): 1–16.
6. Soriano JB, Maier WC, Egger P, et al. Recent trends in physician diagnosed COPD in women and men in the UK. *Thorax* 2000; 55(9):789–794.
7. Prescott E, Vestbo J. Socioeconomic status and chronic obstructive pulmonary disease. *Thorax* 1999; 54(8): 737–741.
8. Wedzicha J, Seemungal T. COPD exacerbations: defining their cause and prevention. *Lancet* 2007; 370(9589): 786–796.
9. Tsoumakidou M, Siafakas N. Novel insights into the aetiology and pathophysiology of increased airway inflammation during COPD exacerbations. *Respir Res* 2006; 7: 80.
10. Hallin R, Koivisto-Hursti U, Lindberg E, Janson C. Nutritional status, dietary energy intake and the risk of exacerbations in patients with chronic obstructive pulmonary disease (COPD). *Respir Med* 2006; 100(3): 561–567.
11. Van Weel C, de Grauw W. Family practices registration networks contributed to primary care research. *J Clin Epidemiol* 2006; 59(8):779–783.
12. Van Weel C. The Continuous Morbidity Registration Nijmegen: Background and history of a Dutch general practice database. *Eur J Gen Pract* 2008; 14 (Suppl 1): 5–12.
13. Research Committee of the Council of the College of General Practitioners. A classification of disease. *J Coll Gen Pract* 1959; 2:140–159.
14. WONCA. An international glossary for primary care. Classification Committee of WONCA in collaboration with the WHO. International Classification of Health Problems in Primary Care-2-defined. 3rd edn. London: Oxford University Press; 1983.
15. Schers H, Bor H, van den Hoogen HJ, van Weel C. What went and what came? Morbidity trends in general practice from the Netherlands. *Eur J Gen Pract* 2008; 14 Suppl 1: 13–24.
16. Van Weel C. Validating long term morbidity recording. *J Epidemiol Community Health* 1995; 49 Suppl 1: 29–32.
17. Van Weel-Baumgarten EM, van den Bosch WJ, van den Hoogen HJ, Zitman FG. The validity of the diagnosis of depression in general practice: is using criteria for diagnosis as a routine the answer? *Br J Gen Pract* 2000; 50(453): 284–287.
18. Bakker B, Sieben I. Maten voor prestige, sociaaleconomische status en sociale klasse voor de standaard beroepenclassificatie 1992. [Measurements for prestige, socioeconomic status and social class for the Standard Classification of Occupations 1992]. *Sociale Wetenschappen* 1997; 40: 1–22.
19. Wilson A, Manku-Scott T, Shepherd D, Jones B. A comparison of individual and population smoking data from a postal survey and general practice records. *Br J Gen Pract* 2000; 50(455): 465–468.
20. Smeele IJ, van Weel C, van Schayck CP, et al. NHG-Standaard COPD [NHG Guideline COPD]. *Huisarts Wet* 2007; 50(8): 362–379.
21. Rabe KF, Hurd S, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med* 2007; 176(6): 532–555.
22. Halbert RJ, Isonaka S, George D, Iqbal A. Interpreting COPD prevalence estimates: What is the true burden of disease? *Chest* 2003; 123(5): 1684–1692.
23. Halbert RJ, Natoli JL, Gano A, et al. Global burden of COPD: systematic review and meta-analysis. *Eur Respir J* 2006; 28(3):523–532.

24. Janssen-Heijnen ML, Nab HW, Van Reek J, et al. Striking changes in smoking behaviour and lung cancer incidence by histological type in south-east Netherlands, 1960–1991. *Eur J Cancer* 1995; 31A(6):949–952.
25. Willemsen MC, van Leent-Loenen HM. Neemt het aantal mensen dat rookt toe of af? [Does the prevalence of smokers decrease or increase?] In: *Volksgezondheid Toekomst Verkenning, Nationaal Kompas Volksgezondheid*. Bilthoven: RIVM, 2007. Available at: http://www.rivm.nl/vtv/object_document/o1210n19085.html (Date last accessed 16 Jun 2009).
26. Bednarek M, Maciejewski J, Wozniak M, et al. Prevalence, severity and underdiagnosis of COPD in the primary care setting. *Thorax* 2008; 63(5): 402–407.
27. Tinkelman DG, Price D, Nordyke RJ, Halbert RJ. COPD screening efforts in primary care: what is the yield? *Prim Care Respir J* 2007; 16(1): 49–53.
28. Van Weel C. Underdiagnosis of asthma and COPD: is the general practitioner to blame? *Monaldi Arch Chest Dis* 2002; 57(1): 65–68.
29. Vandevoorde J, Verbanck S, Gijssels L, et al. Early detection of COPD: A case finding study in general practice. *Respir Med* 2007; 101(3): 525–530.
30. Kessler R, Stahl E, Vogelmeier C, et al. Patient understanding, detection, and experience of COPD exacerbations: an observational, interview-based study. *Chest* 2006; 130(1): 133–142.
31. Wilkinson TM, Donaldson GC, Hurst JR, et al. Early therapy improves outcomes of exacerbations of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2004; 169(12):1298–12303.
32. Langsetmo L, Platt RW, Ernst P, Bourbeau J. Underreporting exacerbation of chronic obstructive pulmonary disease in a longitudinal cohort. *Am J Respir Crit Care Med* 2008; 177(4):396–401.
33. Van der Waart MA, Dekker FW, Nijhoff S, et al. NHG-standaard CARA bij volwassenen: behandeling [NHG Guideline on Chronic Non-specific Lung Diseases in adults: treatment]. *Huisarts Wet* 1992; 35(11): 437–443.



Trends in population burden of COPD: actual facts or fallacies?

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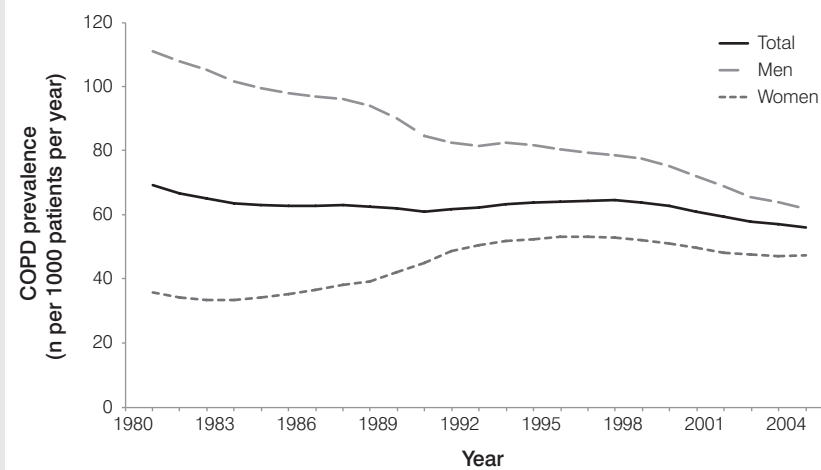
With great interest we read the contribution by Gershon and colleagues¹ about chronic obstructive pulmonary disease (COPD)-related prevalence, incidence, and mortality in Canada. Their study is another example of how administrative databases can be powerful sources of research data. Nonetheless, after studying the article we felt that we should make some comments.

In the time between submission and publication of the article,¹ we have published COPD prevalence data from a primary care database in the Netherlands.² The sex-stratified prevalence trends as reported by Gershon et al¹ contradict our (and others') findings: while their graphs show consistently higher prevalence rates in women, our 30-year trend study shows higher rates in men. Our data clearly show that women are catching up with men in terms of COPD prevalence (Figure), while the figures presented by Gershon et al¹ show the exact opposite. Apart from an error in the male and female labeling in the graphs, we cannot think of a plausible explanation for the remarkable and divergent finding that COPD prevalence is higher in Canadian women.

Our second comment concerns the role of increased physician awareness regarding COPD and its possible impact on prevalence rates when physician-diagnosed COPD is used as an outcome. Indeed, there is little doubt that, with the introduction of many guidelines for diagnosis and management of COPD in the past 10 to 15 years, awareness among physicians will have increased.³ In the "Comment" section, Gershon and colleagues¹ do discuss the effect of this raised awareness in terms of reduced underdiagnosis, but fail to recognize that increased awareness may lead to less false-positive COPD diagnoses as well. We have recently shown that primary care physicians will change a prior diagnosis of COPD in approximately 35% of cases to another diagnosis (mostly asthma) after having reassessed their patients.⁴

Our final comment is about the societal burden of COPD. Gershon and colleagues¹ stress the importance of information about health care resource use by patients with COPD to support health care workers and policy makers to deal with the burden of the disease. Having information about trends in diagnosed COPD and mortality is indeed important, but we were surprised that the authors did not analyze the most essential cost driver in COPD: exacerbations. Reducing exacerbation rates in patients with COPD is not only a major challenge for health care workers and patients themselves, exacerbations also have a substantial impact on COPD-related health care costs, in Canada⁵ and elsewhere.

Figure 1 Trends in prevalence (number per 1000 patients per year) of physician-diagnosed chronic obstructive pulmonary disease (COPD) by sex; 3-year moving averages for 1980 to 2006.² The overall prevalence of COPD has only slightly decreased over time, but the relative contributions of men and women have clearly shifted at the disadvantage of women. Figure used with permission from the *British Journal of General Practice*.²



Lines start at 1981 (average of 1980, 1981, 1982) and end at 2005 (average of 2004, 2005, 2006).

We would be very interested to learn the view of Gershon and colleagues on these issues.

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References

1. Gershon AS, Wang C, Wilton AS, Raut R, To T. Trends in chronic obstructive pulmonary disease prevalence, incidence, and mortality in Ontario, Canada, 1996 to 2007: a population-based study. *Arch Intern Med* 2010;170(6):560-565.

2. Bischoff EW, Schermer TR, Bor H, Brown P, van Weel C, van den Bosch WJ. Trends in COPD prevalence and exacerbation rates in Dutch primary care [published online November 4, 2009]. *Br J Gen Pract* doi:10.3399/bjgp09X473079.
3. Smith CJ, Gribbin J, Challen KB, Hubbard RB. The impact of the 2004 NICE guideline and 2003 General Medical Services contract on COPD in primary care in the UK. *QJM* 2008;101(2):145-153.
4. Poels PJ, Schermer TR, Thoonen BP, et al. Spirometry expert support in family practice: a cluster-randomised trial. *Prim Care Respir J* 2009;18(3):189-197.
5. Mittmann N, Kuramoto L, Seung SJ, Haddon JM, Bradley-Kennedy C, Fitzgerald JM. The cost of moderate and severe COPD exacerbations to the Canadian healthcare system. *Respir Med* 2008;102(3):413-421.

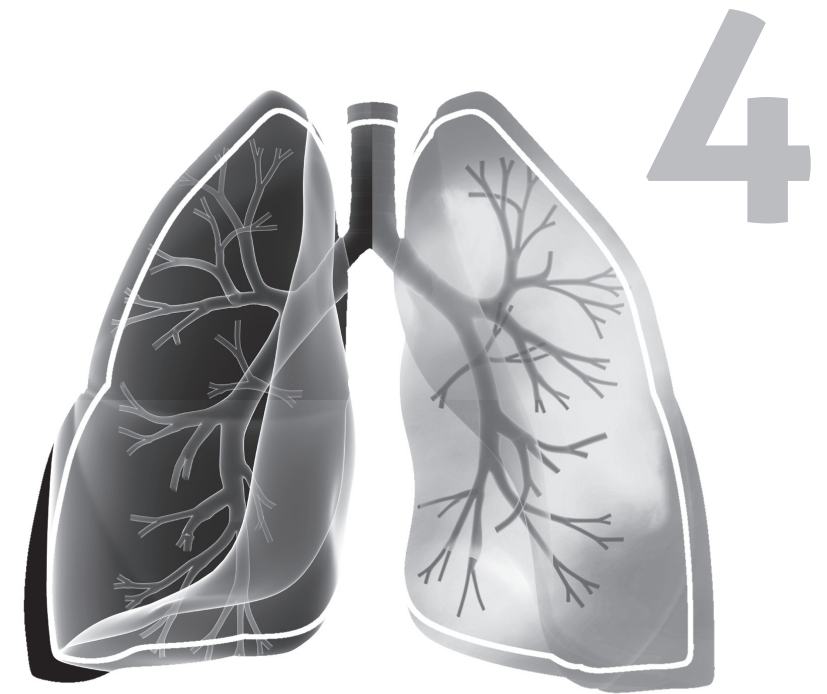
In reply

We thank Bischoff, Crockett, and Schermer for their interest in our article, their insightful comments, and the opportunity to respond to them. They have correctly pointed out that the sex-stratified prevalence trends in Figure 1 of our article¹ have been mislabeled. The male and female labels in the legend have been switched. The data from Ontario, Canada, which is depicted correctly in Table 1 of our article and in the text, agrees with the prevalence trends they described in the Netherlands—specifically, a consistently higher prevalence of COPD in men but also a trend showing that the prevalence in women is catching up with men.² We thank them for pointing out this error. We have informed the Archives, and a correction was published in the June 28, 2010, issue.

With respect to their second comment, we agree that it is possible that increased physician awareness of COPD over time may have led to fewer false-positive diagnoses. This would be consistent with the decreasing incidence of COPD that we observed.¹ Finally, we agree with their observation that exacerbations are a very important outcome to measure and trend in the COPD population. While exacerbations were not the focus of this article, it is an area we are working on for a future publication.

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1. Gershon AS, Wang C, Wilton AS, To T. Trends in chronic obstructive pulmonary disease prevalence, incidence, and mortality in Ontario, Canada, 1996 to 2007 [published correction appears in *Arch Intern Med*. 2010;170(12):1023]. *Arch Intern Med* 2010;170(6):560-565.
2. Bischoff EW, Schermer TR, Bor H, Brown P, van Weel C, van den Bosch WJ. Trends in COPD prevalence and exacerbation rates in Dutch primary care [published ahead of print November 4, 2009]. *Br J Gen Pract* doi:10.3399/bjgp09X473079.



Validity of an automated telephonic system to assess COPD exacerbation rates

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Abstract

Current tools for recording chronic obstructive pulmonary disease (COPD) exacerbations are limited and often lack validity testing. We assessed the validity of an automated telephonic exacerbation assessment system (TEXAS) and compared its outcomes with existing tools.

Over 12 months, 86 COPD patients (22.1% females; mean age 66.5 yrs; mean postbronchodilator forced expiratory volume in 1 s 53.4% predicted) were called once every 2 weeks by TEXAS to record changes in respiratory symptoms, unscheduled healthcare utilisation and use of respiratory medication. The responses to TEXAS were validated against exacerbation-related information collected by observations made by trained research assistants during home visits. No care assistance was provided in any way. Diagnostic test characteristics were estimated using commonly used definitions of exacerbation. Detection rates, compliance and patient preference were assessed, and compared with paper diary cards and medical record review.

A total of 1,824 successful calls were recorded, of which 292 were verified by home visits (median four calls per patient, interquartile range three to five calls per patient). Independent of the exacerbation definition used, validity was high, with sensitivities and specificities between 66% and 98%. Detection rates and compliance differed extensively between the different tools, but were highest with TEXAS. Patient preference did not differ.

TEXAS is a valid tool to assess COPD exacerbation rates in prospective clinical studies. Using different tools to record exacerbations strongly affects exacerbation occurrence rates.

Introduction

Exacerbations of chronic obstructive pulmonary disease (COPD) are acute episodes of sustained symptom aggravation that last from several days to weeks,¹ strongly impair health-related quality of life²⁻⁴ and contribute substantially to COPD-related costs.^{5,6} The burden of exacerbations indicates a growing need to better focus on their prevention and management. Hence, the attention of researchers has shifted from lung function decline as the primary outcome of interest to occurrence of exacerbations.⁷

Despite the emerging importance of exacerbation as a study outcome, there is still no generally accepted definition of exacerbation. Recently, much attention has been paid to the substantial variety in both symptom- and event-based definitions, and, in particular, to the impact of using different algorithms on exacerbation outcomes in clinical trials.^{8,9} So far, surprisingly little attention has been paid to the tools with which exacerbations are actually “measured”. Studies on exacerbation outcomes often fail to provide a detailed description of the precise tools that were used to detect exacerbations. Moreover, exacerbation measurement tools often lack validity testing. Currently, we do not know the impact of using different recording strategies on exacerbation rates. Commonly used methods are based on periodic (retrospective) questionnaires, patient diary cards and medical record review.¹⁰⁻¹² These methods of data collection all have in common that they are rather time consuming for patients and/or researchers, often at the expense of patients' compliance. The introduction of electronic diaries is a promising development,¹³ although their validity should be tested first before they can be recommended for use in clinical COPD research.

In the current study, we assessed the validity of a recently developed automated telephonic exacerbation assessment system (TEXAS) to record exacerbations in prospective clinical studies. We also assessed the system's exacerbation detection rate, patient compliance and patient preference, and compared these outcomes with two conventional exacerbation recording methods, *i.e.* paper diary cards and medical record review. We hypothesised that using different tools to record COPD exacerbations would have an impact on exacerbation rates, even when a uniform definition of exacerbation is applied.

Methods

Study design and population

This study was a 1-yr prospective cohort study in which 86 patients with moderate-to-severe COPD¹⁴ were included. Our cohort size resembled the cohort size used

in the East London, UK studies on exacerbation outcomes.^{1,4} With an expected exacerbation frequency of 2.5 exacerbations per patient per year,¹⁵ the number of patients would be sufficient to obtain meaningful estimates regarding the validity of TEXAS. Recruitment took place between August 2006 and October 2007 in patients who had participated in a previous COPD study¹⁶ or regular pulmonary rehabilitation programmes at the Dept of Pulmonary Diseases (Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands). Inclusion criteria were: chest physician-confirmed diagnosis of COPD in Global Initiative for Chronic Obstructive Lung Disease stage II or III; age ≥ 40 yrs; and no exacerbations in the previous 4 weeks. Exclusion criteria included severe comorbid conditions with a reduced life expectancy, travelling time to the study centre >30 min, inability to speak Dutch, telephone incompatible with system requirements and, in the latter case, patients not willing to switch to another telephone as offered by the investigators. The study was approved by the Medical Ethics Committee (Arnhem-Nijmegen, the Netherlands; approval number 2006/081). All participants gave written informed consent.

TEXAS

We have recently developed TEXAS to record COPD exacerbation-related items in prospective clinical trials. This system consists of questions regarding changes in respiratory symptoms, use of healthcare resources and use of respiratory medication in the 2 weeks prior to the call (see online supplementary material). The questions are based on common and recommended definitions of exacerbation, *i.e.* symptom- and event-based exacerbations.⁸ Once every 2 weeks, a patient with COPD receives an automated telephone call with a real-life voice on the day and time of his/her own preference. If the call cannot be answered a new attempt is made up to four times in the following hour. Prior to the current study, we pre-tested TEXAS in a small group of COPD patients ($n=8$) and healthcare professionals ($n=9$) and, as a consequence, made minor adjustments to the structure and contents of the system.

Study definitions of exacerbation

TEXAS enables researchers to detect exacerbations based on various existing definitions. We used four of the most common and generally accepted definitions of exacerbation, *i.e.* two symptom-based and two event-based definitions (table 1). The symptom-based definitions were based on the concept of major (dyspnoea, sputum purulence and sputum amount) and minor symptoms (common cold, wheeze, sore throat and cough).^{1,17} We used exacerbation definition A as our primary definition, as this is the one most often used definition in COPD studies (it has, for instance, been used consistently in all East London Cohort study reports).^{1,4,18} Definition B has recently been used in studies on the self-treatment of acute

exacerbations.^{19,20} The two event-based definitions were modified from recent landmark COPD trials.^{21–23}

Procedures

Baseline assessment included mapping of demographic characteristics, respiratory symptoms, smoking history, respiratory medication use, and spirometry before and after administration of 400 μg salbutamol *via* a Volumatic® spacer (GlaxoSmith-Kline, Uxbridge, UK). All participants were instructed how to respond to the TEXAS calls, and received a laminated summary card with the precise questions and response categories for the calls. Participants were also instructed how to use a weekly paper diary card (conventional recording method) containing questions about changes in respiratory symptoms, use of respiratory medication and use of unscheduled healthcare services (see online supplementary material). After 2 weeks, participants' experiences with and handling of the TEXAS calls were reviewed, and the formal observation period started. During the study, the results of the calls were monitored on a website that had been specifically designed for the study. This enabled us to contact the patient when two or more consecutive call days showed missing data.

Observations made during home visits by lung function technicians served as gold standard; with the information collected, the responses of the patients to TEXAS could be verified. The technicians were employed at the Dept of Pulmonary Diseases, and were equally experienced in interviewing COPD patients and measuring their lung function. Home visits included spirometry (data not shown), and a standardised interview including questions about changes in respiratory symptoms, use of respiratory medication and unscheduled healthcare utilisation in the preceding 2 weeks. The interviews consisted of more questions than TEXAS, and the questions that were also asked in TEXAS were put in a different order. All calls that met exacerbation definition A were considered positive and were followed by a home visit. For each participant, two randomly selected negative calls were also followed by home visits to serve as negative-control episodes. These visits were scheduled ≥ 4 weeks after a positive call. Home visits were scheduled within 3 days of a positive or negative call. The visiting technicians were not informed whether the call had been positive or negative for an exacerbation.

Copies of patients' medical records were requested from the patients' general practitioners and chest physicians at the end of follow-up. Two investigators (E.W.M.A. Bischoff and J. Molema) independently extracted exacerbations from the combined medical records using standardised exacerbation extraction forms based on the four definitions as displayed in table 1 (interobserver variability: Cohen's k 0.82–0.94). The completed paper diary cards were collected on a monthly basis using prepaid return envelopes. At the end of follow-up, all participants completed a short questionnaire to review their experiences with TEXAS (see online supplementary material).

Analyses

A new exacerbation event was defined as an event that was preceded by 2 weeks in which no major symptoms had changed (symptom-based definitions), or no use of antibiotics and/or prednisolone, or unscheduled physician contacts had been recorded (event-based definitions). Exacerbation recovery was defined as a period of ≥ 2 weeks in which no worsening of any major symptom or use of antibiotics, prednisone or healthcare services was reported after a previous period in which either one or more major symptoms had worsened or oral medication or healthcare services were used. If an event was preceded by missing data, the event was considered as missing and excluded from further analysis.

Common diagnostic test characteristics (sensitivity, specificity, and positive and negative predictive values,²⁴ with 95% confidence intervals) were calculated to establish the diagnostic validity of the TEXAS calls relative to the gold standard, *i.e.* the information collected during the home visits. Diagnostic odds ratios were estimated by logistic mixed models via residual pseudo-likelihood with subject as a random effect. Diagnostic test characteristics and odds ratios were calculated for all four study definitions of exacerbation (table 1). We counted the number of exacerbations recorded by TEXAS, using the paper diary cards and the combined

Table 1 Study definitions of exacerbation

Exacerbation definition	Category	Criteria
A	Symptom-based	A change for at least two consecutive days in either two or more major symptoms (dyspnea, sputum purulence, sputum amount) or any one major symptom plus any one or more minor symptoms (colds, wheeze, sore throat, cough)
B	Symptom-based	A change for at least two consecutive days in two or more major symptoms (dyspnea, sputum purulence, sputum amount)
C	Event-based	A worsening of respiratory symptoms for which the patient initiates a course of prednisolone and/or antibiotics
D	Event-based	A worsening of respiratory symptoms for which the patient pays an unscheduled visit to a general practitioner or a chest physician (including emergency service or outpatient clinic)

medical records for each exacerbation definition. To adjust for the effect of differences in follow-up time, we used a time-weighted statistical approach.²⁵ Exacerbation rates were expressed as number of exacerbations per patient per year, and were compared between TEXAS and the diary cards, and TEXAS and the medical records, using weighted rate ratios.²⁶ Statistical significance was tested using a negative binominal regression analysis.²⁶ Compliance was calculated by counting the complete, incomplete and missing TEXAS calls and paper diaries. Paired t-tests were used to compare patients' compliance and preferences between TEXAS and the diary cards.

SPSS version 16.0.2 (SPSS Inc., Chicago, IL, USA) was used to calculate the diagnostic test characteristics and paired t-tests. SAS version 9.2 for Windows (SAS Institute Inc., Cary, NC, USA) was used for regression analyses. We considered $p < 0.05$ as statistically significant.

Results

Study population

Of the 86 patients enrolled in the study, five (5.8%) patients withdrew their participation during the observation period (fig. 1). The total time of follow-up was 4,226 weeks, or 49.1 weeks per patient. Table 2 shows the characteristics of the study population at baseline. The majority of the patients were male. Most patients were ex-smokers, and were using a combination of a long-acting bronchodilating agent and an inhaled corticosteroid.

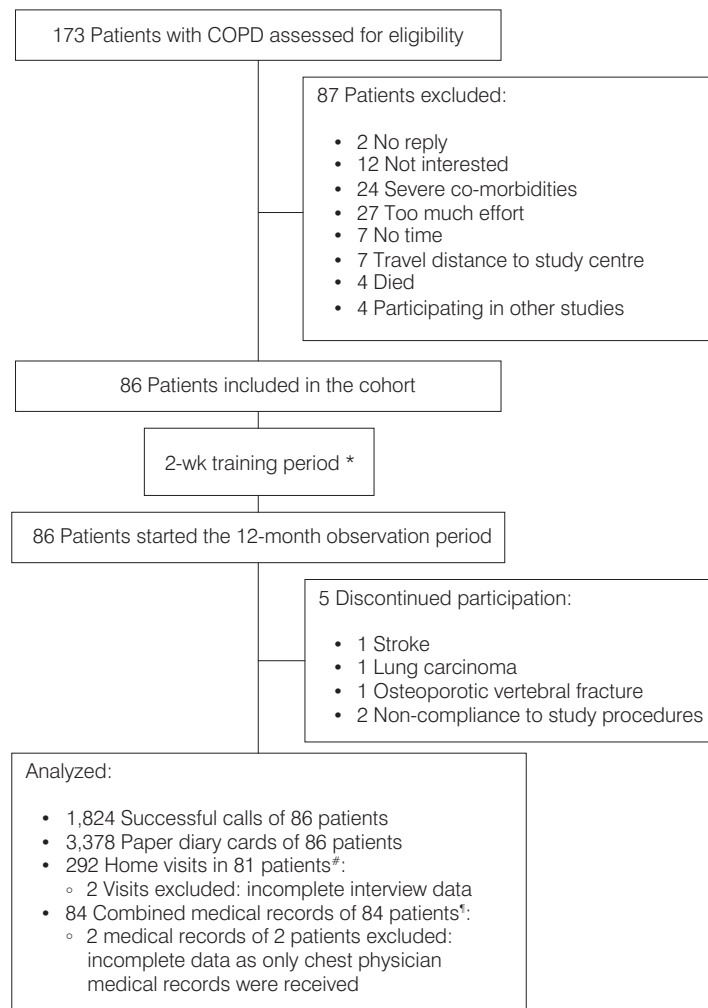
Process of TEXAS calls

Overall, 2,850 call attempts were made on 2,078 scheduled call days (mean \pm SD 24.2 \pm 3.8 call days per patient). On 1,572 (75.6%) days, a call received input from the patient at the first attempt; on 252 (12.1%) days, input was received after several attempts; and on 254 (12.2%) days, there was no input.

Reasons for not providing input were hospitalisation (11 call days), not willing to be called during holidays (43 call days), not able/ willing to answer the call (26 call days) or unknown (174 call days). So, a total of 1,824 (87.8%) call days resulted in useful data entry and were therefore considered successful. The mean \pm SD duration of a successful call was 192.8 \pm 45.6 s.

Validity of TEXAS

81 patients received 292 home visits (median of four visits per patient, interquartile range three to five visits per patient). Five patients did not report any symptom changes that matched exacerbation definition A during their observation period.

Figure 1 Flow chart of participants in the study

* The training period enabled participants to become familiar with responding to TEXAS and completing the paper diaries. After two weeks, participants' experiences with and handling of the TEXAS calls and the paper diaries was reviewed and the formal observation period started.

5 patients did not report any symptom changes that matched exacerbation definition A.

* of 2 patients both chest physician and general practitioner medical records were missing.

Table 2 Baseline characteristics of the study population (n=86)

Characteristic	Data at baseline
Age, years	66.5 (8.7)
Female	19 (22.1%)
Current smoker	13 (15.1%)
Post-BD FEV1 (L)	1.53 (0.56)
Post-BD FEV1 (% of predicted)	53.4 (17.4)
Post-BD FEV1/FVC	42.2 (11.8)
MRC dyspnea score	
1/5	24 (29.6%)
2/5	21 (25.9%)
≥ 3/5	31 (38.3)
BMI, kg/m ²	26.0 (4.1)
Comorbidities	
Cardiac disease	16 (19.8%)
Musculoskeletal disorders	8 (9.9%)
Psychiatric disorders	3 (3.7%)
Respiratory medication	
Only SABA	2 (2.4%)
LABA or ICS	15 (18.3%)
LABA and ICS	65 (79.3%)

Data are presented as mean (SD) or number (%). *Abbreviations:* post-BD FEV1= forced expiratory volume in 1 second after bronchodilation; post-BD FEV1/FVC= ratio of the forced expiratory volume in 1 second after bronchodilation and the forced vital capacity after bronchodilation; MRC=Medical Research Council; BMI=Body Mass Index; SABA=short acting bronchodilator; LABA=long acting bronchodilator; ICS=inhaled corticosteroid

Two home visits were excluded due to incomplete interview data. Mean±SD time between date of the TEXAS call and date of the home visit was 2.3±1.4 days. 190 (65.1%) home visits were scheduled following a call that met exacerbation definition A. In 156 (82.1%) of these visits, the interview data matched the responses of the patients to TEXAS. Table 3 shows the diagnostic test characteristics of TEXAS using the various study definitions of exacerbation. Regardless of the definition used, sensitivity and specificity of TEXAS were high and varied between 66.2% and

97.8%. Sensitivity was lowest and specificity was highest when using exacerbation definition D. Diagnostic odds ratios were high, but highest when using event-based definitions.

Table 3 Diagnostic test characteristics (95% Confidence Intervals) of TEXAS with home visits as 'gold standard', using different definitions of exacerbation

Exacerbation definition	Sensitivity, %	Specificity, %	PPV, %	NPV, %	DOR
Symptom-based					
Definition A [#]	91.2 (85.7 – 94.8)	71.4 (62.3 – 79.1)	82.1 (75.7 – 87.1)	85.0 (76.1 – 91.1)	26.0 (13.4 – 50.6)
Definition B [†]	84.5 (76.1 – 90.5)	82.8 (76.3 – 87.8)	75.0 (66.3 – 82.1)	89.8 (83.9 – 93.8)	26.3 (13.7 – 50.3)
Event-based					
Definition C [§]	81.5 (68.1 – 90.3)	94.9 (91.1 – 97.2)	78.6 (65.2 – 88.0)	95.7 (92.1 – 97.8)	82.5 (33.4 – 203.8)
Definition D [§]	66.2 (53.3 – 77.1)	97.8 (94.6 – 99.2)	89.6 (76.6 – 96.1)	90.9 (86.4 – 94.1)	86.4 (30.8 – 242.1)

PPV = positive predictive value; NPV = negative predictive value; DOR: diagnostic odds ratio

[#]: change for at least two consecutive days in either two or more major symptoms (dyspnea, sputum purulence, sputum amount) or any one major symptom plus any minor symptom (wheeze, sore throat, cough, symptoms of common cold);

[†]: change for at least two consecutive days in two or more major symptoms (dyspnea, sputum purulence, sputum amount);

[§]: initiation of prednisolone and/or antibiotics for a worsening of respiratory symptoms

[§]: unscheduled contact with physician for worsening of respiratory symptoms

Comparison of TEXAS with other tools

At the end of follow-up, 3,378 diary cards, 82 (95.3%) general practitioner medical records and 84 (97.7%) chest physician medical records were received. 15.9% of the exacerbations documented in the medical records lacked any data about changes in major or minor respiratory symptoms. Table 4 shows the exacerbation rates for the different detection methods as well as the rate ratios for TEXAS relative to the paper diary cards and medical record review. Compared with the diary card method, counting exacerbations with TEXAS resulted in statistically significant higher occurrence rates for definitions B and C. Also, TEXAS revealed more

Table 4 Exacerbation rates and Rate Ratio's of TEXAS compared with paper diary cards and medical record review

Exacerbation definition	Exacerbation rate per patient per year			Rate ratio (95% CI)	
	TEXAS	Diary card	Medical record review	TEXAS vs Diary card	TEXAS vs Medical record
Symptom-based					
Definition A [#]	3.21	2.96	0.85	1.08 (0.98 – 1.20)	3.49 (2.60 – 4.70)
Definition B [†]	2.93	2.18	0.42	1.35 (1.17 – 1.55)	6.50 (4.39 – 9.63)
Event-based					
Definition C [§]	1.95	1.69	1.58	1.17 (1.00 – 1.36)	1.29 (1.06 – 1.58)
Definition D [§]	1.54	1.36	1.81	1.14 (0.99 – 1.32)	0.88 (0.73 – 1.07)

[#]: change for at least two consecutive days in either two or more major symptoms (dyspnea, sputum purulence, sputum amount) or any one major symptom plus any minor symptom (wheeze, sore throat, cough, symptoms of common cold);

[†]: change for at least two consecutive days in two or more major symptoms (dyspnea, sputum purulence, sputum amount);

[§]: initiation of prednisolone and/or antibiotics for a worsening of respiratory symptoms

[§]: unscheduled contact with physician for worsening of respiratory symptoms

exacerbations with two or more major symptom changes (definition B) that were not reported to healthcare professionals, compared with the diary cards (47.4% versus 37.6%, respectively). Compared with the medical record review method, TEXAS resulted in significantly higher exacerbation rates for definitions A, B and C.

Table 5 displays patients' compliance with and preferences for TEXAS compared with the diary cards. Overall, compliance with TEXAS was higher than with the diary cards, *i.e.* more registration weeks and more weeks with complete data. The difference in the mean number of weeks with complete registration per patient was almost 1 month in the 12-month observation period. 76 (88.4%) patients responded to the questionnaire about patients' experiences with TEXAS. Most patients (96.5%) found TEXAS easy to use (data not shown), but no significant differences in patients' preferences were observed.

Table 5 Patient compliance and preference comparing TEXAS with diary cards

Compliance	TEXAS	Diary cards	Difference
Total number of registration weeks (% of total follow-up)	3,648 (86.3)	3,378 (79.9)	270 (6.4)
Total number of weeks with complete registration (% of total follow up) [§]	3,642 (86.2)	3,241 (76.7)	401 (9.5)
Mean number of registration weeks per patient (SD or 95% CI)	42.4 (9.3)	39.3 (11.1)	3.1 (2.0 to 4.2) [#]
Mean number of weeks with complete registration per patient (SD or 95% CI)	42.3 (9.3)	38.6 (9.9)	4.08 (3.1 to 5.1) [#]
Patient preference [§]			
Satisfaction, mean (SD) score [¶]	1.45 (1.51)	1.49 (1.45)	-0.04 (-0.26 to 0.18) [*]
Preference, Number of patients (% of total)	17 (22.4)	14 (18.4)	3 (3.5)

[§] Complete registration was defined as no missing data in the questions regarding changes in major and minor symptoms
[§] Data was available of 76 patients
[¶] Score was measured on a 7-point Likert scale varying from -3 (I don't like it at all) to 3 (I like it very much). Score 0=neutral
[#] p < 0.001
^{*} p = 0.720

Discussion

We assessed the validity of TEXAS to record COPD exacerbations in prospective clinical studies, and compared its detection rate, compliance and patient preference with conventional recording methods (weekly paper diary cards and medical record review). The validity of TEXAS was high, independent of the exacerbation definition used. Detection rates and patients' compliance in providing exacerbation-related information differed significantly between the recording strategies, but were highest with TEXAS. Patient preference did not differ significantly between TEXAS and the paper diary cards.

When assessing the validity of any instrument, deciding on the gold standard (*i.e.* the generally accepted method to measure the outcome) is crucial.²⁷ TEXAS was developed to record exacerbations based on common definition criteria, such as symptom changes or events.⁸ Consequently, we used as our gold standard the information on worsening of symptoms, use of oral medication and/or use of healthcare services that was collected by standardised personal interviews by well-trained professionals during home visits. We believe that this was (and still is) the best available procedure to address our primary study objective.

As the definition of exacerbation has an impact on the effect size of interventions,^{8,9} we assumed that it would also affect the validity of our detection method. Therefore, we used four different but commonly used definitions of exacerbation. Overall, the validity of TEXAS was high, but it did differ between the respective exacerbation definitions. Positive predictive values varied between 75% (symptom-based definition) and 90% (event-based definition), which indicates a potential, but small, number of false-positive exacerbations, particularly when using symptom-based definitions. With negative predictive values of >85%, only a few true exacerbations will be missed. The differences in sensitivity suggest that patients were more prone to record symptom changes than use of healthcare services (sensitivity of 91.2% *versus* 66.2%, respectively), which makes TEXAS less suitable to detect this type of event-based exacerbation. The differences in specificity suggest that patients may perform better in recording the absence of healthcare utilisation than the absence of symptom deterioration (specificity of 97.8% *versus* 71.4%, respectively).

To further evaluate the validity of TEXAS, our results should be compared with other studies. Recently, the Exacerbations of Chronic Pulmonary Disease Tool (EXACT) patient-reported outcome (PRO) electronic diary has been developed to measure exacerbation frequency, duration and severity.²⁸ EXACT-PRO introduces a new concept of exacerbation, which makes it the best available method to give insight into the clinical course of an exacerbation. However, exacerbations measured with EXACT-PRO cannot simply be compared with exacerbations based on other definitions. Obviously, this is a benefit of TEXAS; its content has been based on existing and commonly accepted definitions of exacerbation. However, unlike EXACT-PRO, TEXAS fails to provide detailed information on the precise duration and day-to-day clinical course of an exacerbation.

We demonstrated that the use of different detection methods can result in different exacerbation rates. This is important information in view of the interpretation of studies that use exacerbation rates as an outcome. The low number of symptom-based exacerbations retrieved from the medical records should be interpreted with caution, as the general practitioners and chest physicians were not instructed *a priori* how to record symptom-related items. Also, when defining exacerbation as the use of prescriptions of antibiotics and/or prednisolone, exacerbation rates were

lowest with the medical record review method. This may have been caused by the use of standing prescriptions to support exacerbation self-management by patients. With TEXAS, exacerbation rates based on symptoms were much higher than based on unscheduled healthcare utilisation. This is consistent with previous studies that showed that only half of the exacerbations are reported to healthcare professionals.^{1,29}

The higher exacerbation detection rates of TEXAS may be related to the higher compliance rate. With TEXAS, patients had one additional month of complete registration data and, as a consequence, of capturing exacerbations compared with the paper diary cards. We adjusted the exacerbation rate for differences in study follow-up time (time-weighted approach),^{25,26} but believe that adjusting for compliance would provide a better estimate of the exacerbation rate. The high compliance is consistent with a previous study on compliance with paper and electronic diaries,³⁰ and can be explained by the benefits of the system, *i.e.* it requires less self-discipline, patients are called on their preferred day and time, and when using mobile telephones, patients do not have to stay at home. Although not statistically significant, more patients preferred TEXAS compared to the diary cards. A benefit for researchers is the automated data collection, which diminishes the costs usually spent on manual data collection, *i.e.* sending and receiving paper diaries, and manually entering and cleaning data in a database.

In recent years, the use of telephone devices as instruments to capture exacerbations has rapidly evolved in COPD care. Telehealthcare for COPD seems to have the potential to affect the quality of life of patients and the frequency of emergency department visits.³¹ Before we can recommend TEXAS as an instrument for tele-monitoring or self-management purposes (*i.e.* rapid intervention when an exacerbation is imminent), it should be tested in a controlled study that has been specifically designed for this objective.

Our current study has several limitations. First, it may have been affected by bias. Diagnostic suspicion bias was prevented by blinding the technicians who performed the home visits regarding the responses of the patients to TEXAS. However, our results may have been influenced by incorporation bias, as, inevitably, the questions that make up TEXAS were comparable with the questions asked during the home visits. By asking more questions than within TEXAS and by changing the order of the questions during the home visit interviews, we believe that this type of bias has been limited. Second, TEXAS is not a daily dairy card, but measures exacerbations once every 2 weeks. Hence, when using TEXAS, researchers are unable to detect the exact start and end dates of an exacerbation. Additionally, the time-frame of 2 weeks may have introduced recall bias, which may have had more impact on exacerbations based on symptom changes than on the use of healthcare services. Third, with >1,600 negative calls, it was not realistic to perform a home visit after every call that did not meet our exacerbation definition.

Therefore, we verified the absence of an exacerbation in two random negative calls per patient. We believe that this has resulted in an accurate estimate of the diagnostic test characteristics.

In conclusion, this study shows that TEXAS is a valid method to detect exacerbations in prospective clinical COPD studies. Its exacerbation rates and compliance appear to be higher than those of conventional detection methods. The differences in exacerbation rates between the different detection tools indicate that the recording strategy should be taken into account when comparing study results on exacerbation outcomes. Future studies should, therefore, provide at least a detailed description of the exacerbation recording procedure.

References

- Seemungal TA, Donaldson GC, Bhowmik A, et al. Time course and recovery of exacerbations in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2000; 161: 1608–1613.
- Miravittles M, Ferrer M, Pont A, et al. Effect of exacerbations on quality of life in patients with chronic obstructive pulmonary disease: a 2 year follow up study. *Thorax* 2004; 59: 387–395.
- Spencer S, Calverley PMA, Burge PS, et al. Impact of preventing exacerbations on deterioration of health status in COPD. *Eur Respir J* 2004; 23: 698–702.
- Seemungal TA, Donaldson GC, Paul EA, et al. Effect of exacerbation on quality of life in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1998; 157: 1418–1422.
- Wedzicha JA, Wilkinson T. Impact of chronic obstructive pulmonary disease exacerbations on patients and payers. *Proc Am Thorac Soc* 2006; 3: 218–221.
- Wouters EF. Economic analysis of the Confronting COPD survey: an overview of results. *Respir Med* 2003; 97: Suppl. C, S3–S14.
- Burge PS, Calverley PM, Jones PW, et al. Randomised, double blind placebo controlled study of fluticasone propionate in patients with moderate to severe chronic obstructive pulmonary disease: the ISOLDE trial. *BMJ* 2000; 320: 1297–1303.
- Effing TW, Kerstjens HA, Monninkhof EM, et al. Definitions of exacerbations. Does it really matter in clinical trials on COPD? *Chest* 2009; 136: 918–923.
- Trappenburg JCA, van Deventer AC, Troosters T, et al. The impact of using different symptom-based exacerbation algorithms in patients with COPD. *Eur Respir J* 2011; 37: 1260–1268.
- Burge S, Wedzicha JA. COPD exacerbations: definitions and classifications. *Eur Respir J* 2003; 21: Suppl. 41, 46s–53s.
- Hoogendoorn M, van Wetering CR, Schols AM, et al. Is INTERdisciplinary COMMunity-based COPD management (INTERCOM) cost-effective? *Eur Respir J* 2010; 35: 79–87.
- Rutten FH, Zuithoff NP, Hak E, et al. b-Blockers may reduce mortality and risk of exacerbations in patients with chronic obstructive pulmonary disease. *Arch Intern Med* 2010; 170: 880–887.
- Pauwels R, Calverley P, Buist AS, et al. COPD exacerbations: the importance of a standard definition. *Respir Med* 2004; 98: 99–107.
- Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management and Prevention of COPD. Available at: www.goldcopd.org/guidelines-global-strategy-for-diagnosis-management.html Date last accessed: January 2012. Date last updated: December 2011.
- Wilkinson TM, Donaldson GC, Hurst JR, et al. Early therapy improves outcomes of exacerbations of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2004; 169: 1298–1303.
- Boot CR, Vercoulen JH, van der Gulden JW, et al. Sick leave in patients with obstructive lung disease is related to psychosocial and work variables rather than to FEV1. *Respir Med* 2005; 99: 1022–1031.
- Anthonisen NR, Manfreda J, Warren CP, et al. Antibiotic therapy in exacerbations of chronic obstructive pulmonary disease. *Ann Intern Med* 1987; 106: 196–204.
- Donaldson GC, Seemungal TA, Bhowmik A, et al. Relationship between exacerbation frequency and lung function decline in chronic obstructive pulmonary disease. *Thorax* 2002; 57: 847–852.
- Sedeno MF, Nault D, Hamd DH, et al. A written action plan for early treatment of COPD exacerbations: an important component to the reduction of hospitalizations. *COPD* 2009; 6: 352–358.
- Bischoff EW, Hamd DH, Sedeno M, et al. Effects of written action plan adherence on COPD exacerbation recovery. *Thorax* 2011; 66: 26–31.
- Calverley PM, Anderson JA, Celli B, et al. Salmeterol and fluticasone propionate and survival in chronic obstructive pulmonary disease. *N Engl J Med* 2007; 356: 775–789.
- Wedzicha JA, Calverley PM, Seemungal TA, et al. The prevention of chronic obstructive pulmonary disease exacerbations by salmeterol/fluticasone propionate or tiotropium bromide. *Am J Respir Crit Care Med* 2007; 177: 19–26.
- Tashkin DP, Celli B, Senn S, et al. A 4-year trial of tiotropium in chronic obstructive pulmonary disease. *N Engl J Med* 2008; 359:1543–1554.
- Knottnerus JA, van Weel C, Muris JW. Evidence base of clinical diagnosis: evaluation of diagnostic procedures. *BMJ* 2002; 324:477–480.
- Suissa S. Statistical treatment of exacerbations in therapeutic trials of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2006; 173: 842–846.
- Aaron SD, Fergusson D, Marks GB, et al. Canadian Thoracic Society/Canadian Respiratory Clinical Research Consortium. Counting, analyzing and reporting exacerbations of COPD in randomized, controlled trials. *Thorax* 2008; 63: 122–128.
- Grobbee DE, Hoes AW. *Clinical Epidemiology. Principles, Methods, and Applications for Clinical Research*. Massachusetts, Jones and Bartlett Publishers, 2009.
- Leidy NK, Wilcox TK, Jones PW, et al. Standardizing measurement of COPD exacerbations: reliability and validity of a patient-reported diary. *Am J Respir Crit Care Med* 2011; 183: 323–329.
- Langsetmo L, Platt RW, Ernst P, et al. Under-reporting exacerbation of COPD in longitudinal cohort. *Am J Respir Crit Care Med* 2008; 177: 396–401.
- Stone AA, Shiffman S, Schwartz JE, et al. Patient compliance with paper and electronic diaries. *Control Clin Trials* 2003; 24: 182–199.
- McLean S, Nurmatov U, Liu JL, et al. Telehealthcare for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2011; 7:CD007718.

Appendix CHAPTER 4

Online Supplement
Validity of an automated telephonic system
to assess COPD exacerbation rates in prospective clinical studies

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Contents of TEXAS call (translated to English, original questions were in Dutch)*

Introduction:

This call is only meant for Mr./Mrs. ..name.. Are you Mr./Mrs. ..name..?	press 1
Could you please hand over the phone to Mr./Mrs. ..name..?	press 2
Do you want us to call you back on a different day or time?	press 3

The following questions concern your respiratory symptoms:

During the last two weeks, did you experience any events of two or more days on which ...		
1.	... you were shorter of breath than usual?	1=YES / 2=NO
2.	... you had more sputum than usual?	1=YES / 2=NO
3.	... your sputum was different in color or composition than usual?	1=YES / 2=NO
4.	... you experienced more wheezing or your chest felt tighter ?	1=YES / 2=NO
5.	... you had a sore throat ?	1=YES / 2=NO
6.	... you had to cough more than usual?	1=YES / 2=NO
7.	... you had a cold or a runny nose ?	1=YES / 2=NO
8.	... you used more puffs of your bronchodilator than usual?	1=YES / 2=NO
9.	During the last two weeks, did you initiate a course of prednisolone or antibiotics because of a worsening of your respiratory symptoms?	1=YES / 2=NO
10.	Did you experience days on which you were not able to perform your usual daily activities?	1=YES / 2=NO
10.b	On how many days did you experience this?	PRESS THE NUMBER OF DAYS AND END WITH #
11.	During the last two weeks did you need any unscheduled medical attention because of a worsening of your respiratory symptoms?	1=YES / 2=NO
11.b	If so, did you visit your general practitioner (GP)?	press 1
	Or did you visit an Emergency Department?	press 2
	Or did you visit the GP after-hour service?	press 3
	Or did you visit more than one of the above mentioned care providers?	press 4
12.	Do you have any additional information or do you want to leave a message for the researchers? Please note: with this call you cannot ask any question to your doctor	1=YES** / 2=NO

Thank you for answering this call. We will call you back in 14 days.

* Patients received a laminated summary card with the precise questions and response categories for the TEXAS calls
** After pressing '1', patients were able to leave a short spoken message.

Contents of paper diary card

Week 1 – 4

Please fill in this diary card every week on the same day and time. In the week that you are being called by TEXAS, please answer the telephone questions first before you fill in the diary card. Please circle the appropriate answer.

	Week 1	Week 2	Week 3	Week 4
1. Date:				
During the last seven days ...				
3. ... did you initiate a course of prednisolone because of a worsening of your COPD?	yes	no	yes	no
4. ... did you initiate a course of antibiotics because of a worsening of your COPD?	yes	no	yes	no
5. ... did you use more puffs of your bronchodilator than usual ?	yes	no	yes	no
6. ... did you visit your general practitioner (GP) because of a worsening of your COPD?	yes	no	yes	no
7. ... did you visit the GP after-hour service because of a worsening of your COPD?	yes	no	yes	no
8. ... did you visit your lung physician because of a worsening of your COPD?	yes	no	yes	No
9. ... did you visit the Emergency Department because of a worsening of your COPD?	yes	no	yes	no
During the last seven days, did you experience any events of two or more days on which ...				
10. ... you had to cough more than usual?	yes	no	yes	no
11. ... you had a cold or a runny nose?	yes	no	yes	no
12. ... your sputum was different in color or composition than usual?	yes	no	yes	no
13. ... you had more sputum than usual?	yes	no	yes	no
14. ... you had a sore throat?	yes	no	yes	no
15. ... you experienced more wheezing or your chest felt tighter?	yes	no	yes	no
16. ... you were shorter of breath than usual?	yes	no	yes	no

TEXAS Evaluation Form

(translated to English, original questions were in Dutch)

1. Did you find TEXAS easy to use?

- ☐ No
- ☐ Neutral
- ☐ Yes

2. Did you experience any problems with the call system?

(For example, did you experience not being called on the day or time of your preference, that the connection was ended, or that you could not hear the telephone voice?)

- ☐ No
- ☐ Only once
- ☐ More than once
- ☐ Often
- ☐ Very often

3. How do you like being called by TEXAS once every two weeks?

-3	-2	-1	0	1	2	3
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I don't like it at all I like it very much

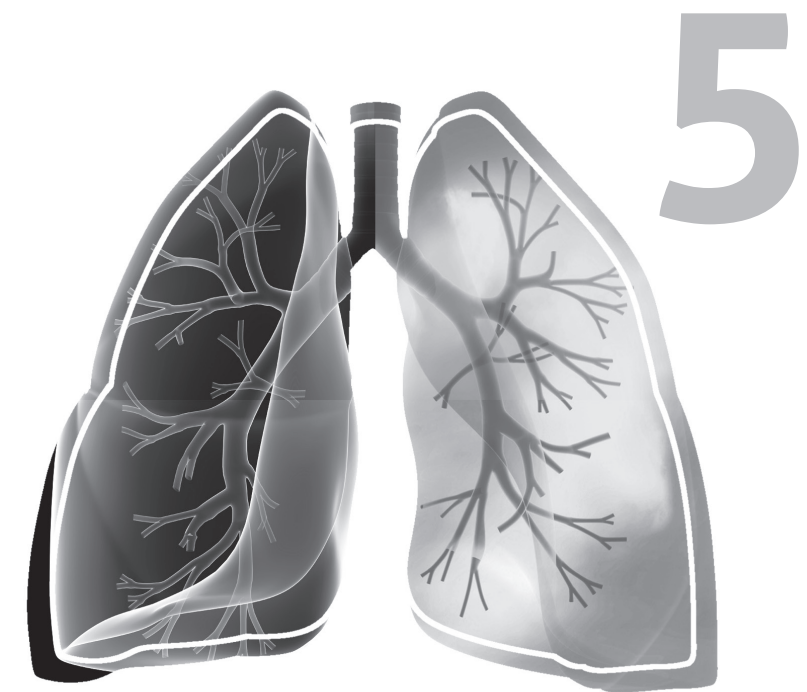
4. How do you like filling in a diary card once a week?

-3	-2	-1	0	1	2	3
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I don't like it at all I like it very much

5. Which method of data collection do you prefer?

- ☐ TEXAS
- ☐ The diary cards
- ☐ No preference



Self-management in prevention and early intervention of exacerbations

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Introduction

Exacerbation of chronic obstructive pulmonary disease (COPD) is usually defined as an acute episode of sustained deterioration of symptoms, i.e., worsening of dyspnea and change in sputum, beyond normal day-to-day variations.¹ Although many exacerbations are successfully managed in primary care, they are yet a common cause of hospital admission, often after failed initial therapy in the community. Exacerbations are severely distressing events that impact greatly on health status, loss of symptom control, and activities of daily life. Frequent exacerbations significantly diminish patients' health status,² and moderate to severe COPD patients have a mean of two exacerbations a year.³ Patients' symptom recovery time varies between 4 and 14 days^{3,4} except that activities of daily living and mental state can take longer to recover, up to 18 and 39 days.⁴ Decreasing the rate of exacerbations is associated with improved quality of life^{5,6} and thus would be expected to reduce hospitalizations and benefit health care costs.⁷ Furthermore, early report and treatment have been shown to reduce the length of an exacerbation, to improve patients' health status, and to decrease hospital admissions.⁸

If we are to progress in the management of COPD exacerbations, treatment goals should not only aim to treat the acute episode but the focus should also be on prevention and early treatment. New strategies that will help patients to recognize their exacerbation and to initiate treatment promptly may have great potential. Self-management education programs with a written action plan that includes rapid access and/or standing prescriptions for antibiotics and/or prednisone in the event of an exacerbation have been proposed as a strategy for early treatment of exacerbations.^{9–11} Such a strategy may be effective in reducing hospital admissions,¹² presumably by decreasing the severity and duration of exacerbations.

In this chapter, the concept and practice of self-management and its potential role in the prevention and early treatment of COPD exacerbation is discussed on the basis of the most recent medical literature. This chapter will give practical advices for implementation of self-management strategies, given rapid access to treatment by the means of a written action plan as an option, and suggestions for future research.

Self-management in COPD

The Self-management Model

Self-management can be described as a set of skilled behaviors and refers to the various tasks that individuals carry out for the management of their condition.¹³ A self-management program in COPD targets the integration of effective interventions

that are recognized to be effective in disease control, such as healthy life habits (smoking cessation, regular exercise) and self-management skills (adherence to medication, breathing techniques and positioning, early recognition and prompt treatment of exacerbations).^{9,14}

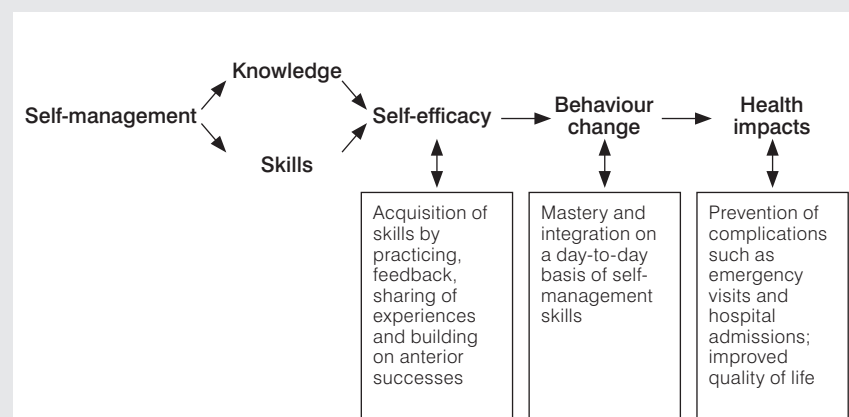
Self-management is not only about education (teaching effective interventions), but it is aiming at behavior modification and maintenance. Self-management in chronic disease requires a process that can be illustrated as a causal chain (Fig. 1). Self-management skills are not enough to bring about change in behavior and produce health impacts. Many so called self-management programs rely on merely passing information to the patient, and consider that success is attained if patient's disease knowledge has improved. A meta-analysis of 30 studies of chronic disease¹⁵ showed that efforts to improve health by improving knowledge alone were rarely successful, meaning that people may memorize information well, but are not necessarily able to put the information into use. Behavioral-oriented programs (regimen-oriented) and sustainability in the education process are consistently more successful at improving the clinical course of chronic disease. These are keys to the success of any self-management education program.

Improving disease knowledge is one important target, but it is only the beginning of the process. In a chronic disease such as COPD, it is important to work at improving patients' confidence in their own ability to modify and maintain a specific behavior. A self-management program should be designed to increase self-efficacy (Fig. 1), which is the individual's belief in his or her ability to execute necessary actions in response to specific situations. Self-efficacy is task related and is considered in the social cognitive theory¹⁶ a predictor of behavioral change; individuals choose and invest the effort to maintain a specific action only if they believe that they are capable of doing it and will benefit from it. The limited numbers of studies evaluating the role of self-efficacy in COPD have consistently reported it as a significant predictor of adherence to exercise programs and pulmonary rehabilitation.^{17,18} There is also indication that a self-management program can result in lifestyle changes. In a qualitative study by Nault and colleagues,¹⁹ the majority of COPD patients educated via the self-management program "Living Well with COPD" reported experiencing lifestyle modifications, such as learning to breathe and maintaining exercise. It is only when the new behaviors have been mastered and integrated to the patient's daily life that we could expect improvements on health status and health care utilization.

Self-management and high-quality chronic disease care

The chronic care model has been a proposed solution for effective management of patients with chronic diseases. This model identifies essential elements that encourage high-quality chronic disease care: (i) self-management approach, (ii)

Figure 1 Effective chronic illness care model—self-management.
Source: Adapted from Ref. 13.



delivery system design, (iii) decision support, and (iv) clinical information systems.²⁰ Self-management interventions include education, behavioral support, and motivation. The care delivery system must be designed to provide "advanced" access to chronic care. Patient interactions with an integrated team that includes a skilled health professional who acts as "case manager" are a key component. Therapies given should be based on evidence-based practice guidelines, and support from specialists must be assured. The final component of the chronic care model, which is often lacking, involves integrating a computerized clinical information system into clinical practice to plan care, implement automated reminders to comply with clinical guidelines, and provide individual feedback to care providers regarding their performance.¹⁴ The four components of the chronic care model are not independent. A recent systematic review by Adams²¹ suggested that implementing an intervention that includes at least two of these components is an effective preventative strategy to reduce health care use in COPD, while interventions that only apply one of the components (self-management without the delivery system and decision support) will not have a clear benefit on outcomes such as emergency department visits and hospital admissions.

This is why one of the minimum requirements for implementing a successful self-management education program is to have a continuum of care which includes access and continuous communication with a case manager, as already shown in chronic diseases such as arthritis and diabetes.^{22–24} A case manager within a mul-

tidisciplinary care team ensures that some critical elements of care that physicians may not have the training or time to do are competently performed.²⁵ In self-management programs, case managers are used to empower patients with the knowledge and skills necessary to manage their own illness and, more importantly, to gain the confidence to apply these skills on a daily basis²⁶ by using various strategies such as practice, feedback, reattribution of the perceived causes of failure, and role modelling.¹³ Case managers evaluate patient comprehension, beliefs, and self-efficacy throughout the self-management program, while making sure those healthy behaviors and self-management skills are integrated. Case managers play an important role in facilitating and coordinating care activities, monitoring patient's progress, and modifying the delivery of services as needed.

Self-management effectiveness

When studying the literature on self-management, several trials have described the effects of self-management strategies on COPD exacerbations. With regard to the model of self-management, these studies show major differences in intensity of the programs, educational processes, and role of care providers. In addition, studies often have methodological limitations in statistical power, sustainability of the education program, and outcomes measured, which makes it difficult to compare the trials and may explain their failure to show positive results.²⁷ Usually, no information is provided on patient self-efficacy or on methods used to enhance it as part of the self-management education program. Many of these studies may have simply failed to intervene. Instead of pooling the results of individual trials, it is perhaps of more interest to scrutinize the few successful interventions and explain their success by using the self-management model.

The Canadian Living Well with COPD program was one of the first self-management interventions, which clearly demonstrated a significant reduction in health care use and an improvement in health status,²⁸ even after a two-year follow-up period.²⁹ These results were confirmed by a self-management intervention from New Zealand³⁰ and an integrated care plan tested in Spain and Belgium.³¹ The latter has also been demonstrated to improve COPD knowledge, exacerbation identification and early treatment, as well as inhaler adherence and proper use.³² The contents of these programs are similar to those with inconclusive results;^{33,34} they mainly focus on proven effective topics, such as smoking cessation, accurate use of medication, promotion of exercise, and early recognition and treatment of exacerbations. However, in the successful programs the education plan was customized to each individual patient and aimed at enhancing self-efficacy and behavior modification by setting achievable goals. The self-management strategies were embedded in an integrated health care system coordinated by a case manager who provided a continuum of care throughout the follow-up period. By

regular contacts with the patient, the case manager ensures the maintenance of self-management skills, provides empowerment, and is able to respond to changes in the trajectory of the disease.

Self-management to prevent exacerbation

Preventing acute exacerbations in COPD should be as important as it is to prevent myocardial infarction in patients with cardiovascular disease. Behavioral interventions based on the self-efficacy theory, such as self-management, show enormous potential as part of the continuum of care to improve adherence to preventive strategies for acute exacerbations such as smoking cessation, vaccination, and regular pharmacotherapy.

Poor adherence in patients with COPD entails risk of adverse health outcomes, including suboptimal treatment leading to COPD exacerbations, emergency department visits, and hospitalizations. Making sure patients are adherent to their therapy should be as important as prescribing the right medication. Important lessons have been learned from COPD and other chronic disease self-management programs. For example, providing information in both written and oral forms and allowing an opportunity for discussion can increase knowledge and adherence.^{35,36} The effectiveness of counseling is maximized when information is presented in a structured manner over a period of at least 15 minutes. Interventions that include prescribed behavioral components (e.g., keeping medications in one place, self-monitoring of symptoms, and medication use, etc.) are more effective.

Self-management groups led by professional staff or trained lay patients can provide a cost-effective^{29,35–38} and enjoyable way for patients to learn about managing their disease and rehearse^{13,39} new behaviors while receiving support from other families and patients with COPD.

Having opportunities to regularly discuss the use of self-management strategies and problem-solving skills with the physician and the case-manager enhances patient self-efficacy, and it is also of great importance.

Self-management and early treatment

Importance of early treatment

To date, treatment has focused mostly on therapy to decrease admissions, reduce length of hospital stay, and hasten recovery. More attention needs to be paid to the early treatment of exacerbations to prevent complications such as deterioration in quality of life and hospitalizations. However, to be able to intervene early, patients have to recognize and to report promptly their symptoms. Under-reporting of COPD

exacerbations seems to be a widespread phenomenon, as 30% of patients have problems in recognizing warning signs when an exacerbation is imminent⁴⁰ and less than 50% of patients report to the health care provider.^{3,4}

Failure to report exacerbations has been shown to be associated with an increased risk of emergency hospitalization⁸ due to a delay or a failure in treatment. Unreported exacerbations are very similar with reported exacerbations in terms of severity and duration of symptoms and changes in lung function.³ Although unreported exacerbations may not be serious enough to warrant an emergency visit or hospitalization, they may still have an important impact on health status for a given patient.⁴¹ The high incidence of unreported exacerbations may indicate an unmet health care need. Improving patient understanding of the nature of an exacerbation and improving early recognition of its symptoms could benefit reporting and early treatment. Patient recognition of exacerbation symptoms and prompt treatment has been shown to improve exacerbation recovery, reduce risks of hospitalization, and it is associated with better health status.⁸

Use of tailored action plans

Early treatment of exacerbations can only be accomplished when patients undertake immediate actions to respond to changes in their baseline symptoms. This requires knowledge of exacerbations, skills for proper management, and self-confidence to start prompt action. Action plans, whether embedded or not in a comprehensive self-management intervention, are useful in providing the patient a guideline for proper management of an exacerbation. Although early treatment is mainly focused on appropriate medication changes, an action plan is more than simply prescribing the use of rescue medication, antibiotics, or oral prednisone. An action plan should include key components that will facilitate patients managing the exacerbation, such as recognition of symptom deterioration, medication to be adjusted or added depending on symptoms presentation, proper response timing, resources to contact, and other important self-management strategies to be applied and/or maintained in case of exacerbation (e.g., breathing and relaxation techniques). In addition, action plans should include a section in which the baseline symptoms are identified and the actions to remain stable are addressed (e.g., healthy lifestyle and medication compliance). Table 1 shows the essential components of a written action plan and required skills for the prevention and early treatment of COPD exacerbations.

The use of an action plan also requires a proper delivery structure with support by a case manager to assure that the response to treatment is adequate and to promote long-term adherence case managers should be accessible to patients, and, if possible, provide a close follow-up at the time of an exacerbation (Fig. 2). As with any other skill, patients experience a learning curve, and need to practice on

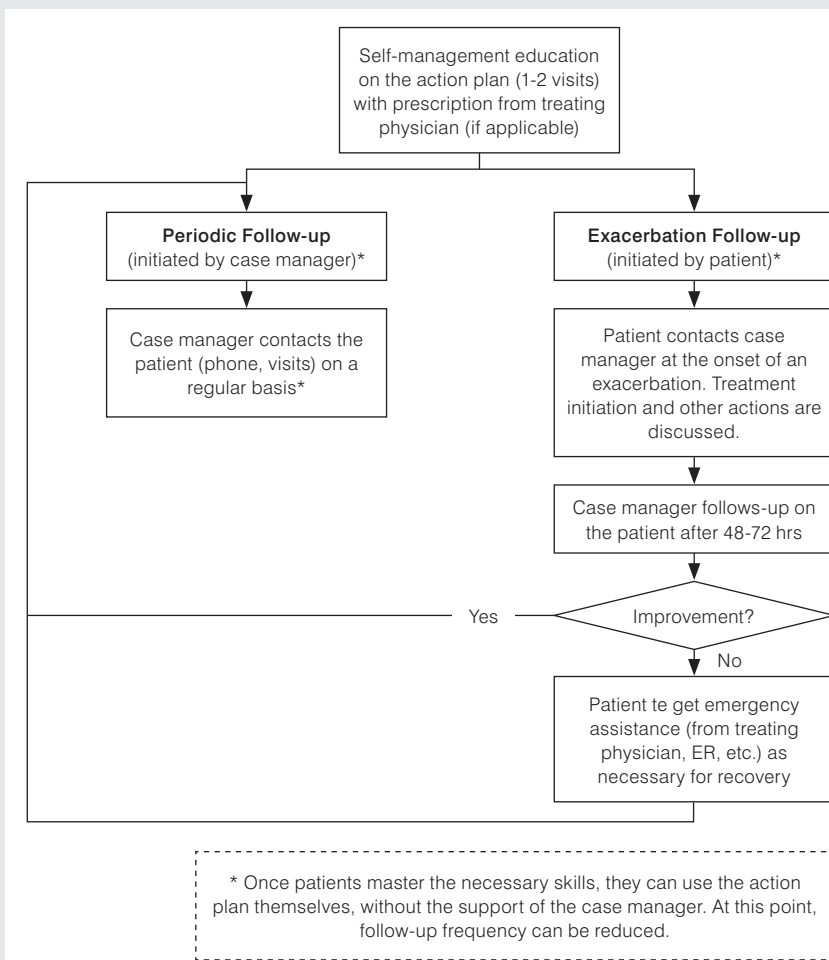
Table 1 Essential components of a written plan of action and required skills for the prevention and early treatment of COPD exacerbations

Component	Required self-management skill
How to remain stable and prevent exacerbations	Knowledge of baseline symptoms Adherence to medication Maintenance of healthy behaviors (e.g., healthy diet, quit smoking, exercise) Identification and avoidance of factors that make symptoms worse (e.g., indoor and outdoor pollutants, emotions, changes in temperature, respiratory infections)
How to manage an acute exacerbation	Recognition of symptoms deterioration Knowledge of contact resources (case manager) Knowledge of medication to be increased or added depending on symptom presentation and within recommended delay Use of breathing, relaxation, and energy conservation techniques
How to manage a non-improvement or worsening of exacerbation	Recognition of non-improvement or worsening in symptoms within expected delay Knowledge of contact resources (case manager, treating physician, emergency department)
How to manage an emergency situation regarding the exacerbation	Recognition of life-threatening symptoms Knowledge of contact resources (emergency services)

using their action plans. Case managers help patients in this process, building on previous success to improve self-confidence, and reassuring them when bad experiences occur. In this way, the action plan becomes a streamlined intervention that summarizes the full self-management education program.

Individualized action plans have been shown to help patients recognize and react appropriately to an exacerbation by promptly self-initiating antibiotics and oral steroids.⁴² Although the studies showed that patients provided with an action plan have a better knowledge of the importance of early intervention and how to implement appropriate treatment for an exacerbation, they could not show benefit in reducing health service use. New study results suggest that a written action plan embedded in a comprehensive self-management intervention can considerably

Figure 2 Action plan follow-up process as part of a self-management education program: shared decision-making and close follow-up during the event of an exacerbation, as well as planned contacts are necessary to assure proper response to treatment and to promote long-term adherence.



contribute to reduce health care utilization.⁴³ The use of action plans to help patients recognize symptom changes, to implement self-care behaviors, and to promptly self-initiate a customized prescription in the event of an exacerbation is a promising strategy.

Practice advice in using an action plan

Since its development in 1996, much experience has been gained with the implementation of the self-management program Living Well with COPD. The program has been evaluated,²⁸ adjusted to meet the needs of health care professionals and patients, and approved by the health ministry in Québec, Canada. Nowadays, most of the health professionals in Québec use this evidence-based program to educate their COPD patients. The full educational material as well as reference guides describing its implementation (individual and group education) can be found on the website www.livingwellwithcopd.com (password: copd).

One of the patient learning modules specifically addresses the use of a tailored action plan for acute exacerbations. The matching reference guide describes a step-by-step process in which the health professional (case manager) guides the patient in the learning process (Table 2). At first, the case manager evaluates patient's present knowledge and behaviors (e.g., understanding of exacerbations and actions taken to prevent or manage them). By doing this, the case manager is able to identify patients' learning needs. Subsequently, each of the session's topics is discussed; e.g., importance and structure of an action plan, recognition of an exacerbation, and actions to manage it. The reference guide identifies learning objectives for each topic and suggests questions to evaluate patient comprehension and beliefs, identify barriers, and solutions to them. The educational session ends with an evaluation of the patient's self-efficacy (beliefs with respect to the value of an action plan and own capabilities to use it). Additional references are described; in this case, the case manager should communicate with the treating physician to discuss rapid access and/or the use of a self-administered prescription.

The case manager should remain accessible to the patient for support and close follow-up at the time of an exacerbation (Fig. 2). In addition, at periodic scheduled telephone calls, the case manager reviews the patient's general health condition and the use of self-management strategies to reinforce the acquired skills. When the patient demonstrates a complete integration of the appropriate skills to manage an exacerbation, the role of the case manager has been fulfilled.

Conclusion

Providing COPD patients with the self-management skills they need to properly manage their COPD should be considered as important as writing the correct prescription. Besides enhancing patient self-efficacy as part of self-management education, shared decision-making during the initial and regular follow-up is also important to promote long-term adherence.

Table 2 Structure of the educational session on the action plan (Living Well with COPD): Interventions and suggested questions

Interventions	Suggested questions
1. Explore present patient's knowledge and behaviors	According to you, what is a COPD exacerbation? What do you usually do when your symptoms get worse?
2. i. Present/demonstrate technique/discuss topic	Why should you use an action plan? What is included in an action plan?
ii. Evaluate patient's comprehension	Who are your resource persons, how and when should you contact them? Could you describe your daily symptoms? What should you do to keep your health condition stable? Which changes in your COPD symptoms tell you that you may have a respiratory infection? When should you start your additional treatment? How do you know that your symptoms improved? What should you do if you feel you are in danger?
3. Explore possible barriers to integration of skills and behaviors learned	What prevents you from using your action plan?
4. Evaluate patient's level of self-efficacy	Do you believe that you will be able to use your action plan to prevent or manage an exacerbation at home? Do you believe that an action plan can help to prevent or manage a worsening of COPD symptoms?
5. Reference to other health professionals if needed	Did you get your prescription from your physician? Is your action plan prescription on file at the pharmacy?

Source: Adapted from Ref. 45

The use of action plans to help patients recognize symptom changes, to implement self-care, and to self-initiate a customized prescription (antibiotics and corticosteroids) in the event of an exacerbation has been suggested as a promising strategy. So far, there is growing evidence that self-management influences COPD

exacerbation management and decreases health care utilization. Successful programs are based on organization and practice that include accurate self-management strategies, enhance patients' self-efficacy and specific skills, and are supported by a practice team and a case manager to optimize disease control and follow-up. Studies have shown that patients can learn how to recognize symptom changes and to react promptly. The results of effective studies show that implementation of self-management programs and written action plans in primary and secondary care is possible. However, well-designed and adequately powered studies are still needed to strengthen the positive results and to resolve remaining questions.

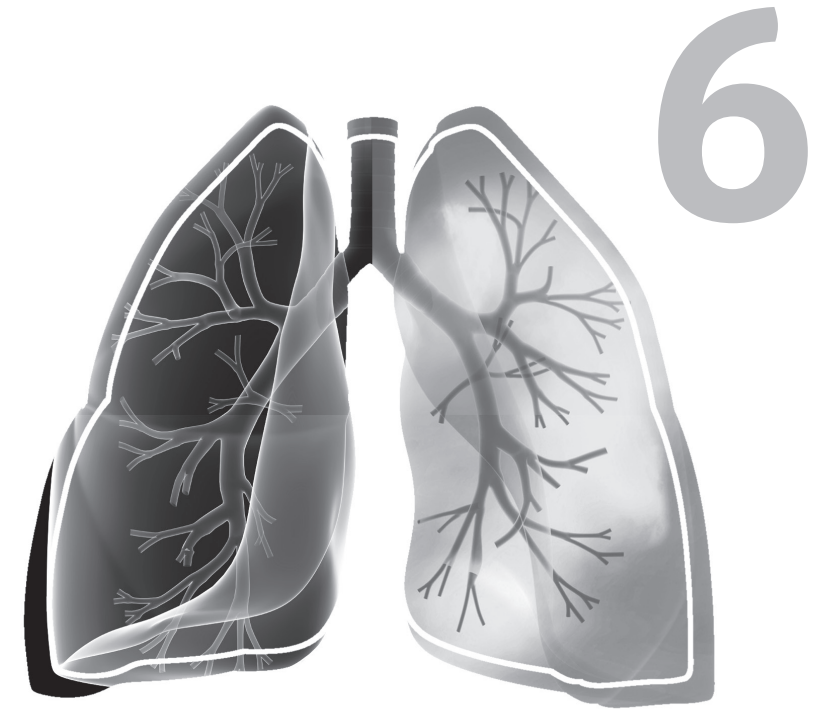
Needs for research

Further research is undoubtedly needed to strengthen the results of the positive studies on which current guidelines are mainly based. Research needs to be carried out to gain insight on health behavior change interventions in COPD in order to design more effective self-management programs. For future studies it is imperative to realize that a self-management strategy must enhance self-efficacy and behavior modification before it can affect exacerbation outcomes. Therefore, self-efficacy and behavior modification should be measured as outcomes. Future clinical trials need to be planned and designed more carefully; studies should be powered properly.

Furthermore, future studies must avoid the methodological pitfalls, which might have caused equivocal and inconclusive results in previous studies. Benefits of a self-management program on health care utilization and health status are more likely to be observed in a study population consisting of patients with moderate to severe COPD, and previous hospitalization due to exacerbations. Only few studies consider comorbidities as possible confounders, whereas depression and anxiety can inhibit self-management.⁴⁴ A recent review on the effects of action plans demonstrated that exacerbation severity and duration were not used as outcomes in any of the reviewed trials.⁴² This is conspicuous, as early symptom recognition and prompt treatment of exacerbations affect health care utilization and health status by decreasing the severity and length of an exacerbation. If we are to progress in the management of acute exacerbation, it is evident that the effect of early interventions on symptom recovery and health status should be considered as an essential component of clinical trials.

References

- Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease: NHLBI/WHO workshop report, updated 2005. Bethesda, MD: National Heart, Lung and Blood Institute, 2005. Available at: www.goldcopd.com/download.asp?intID_231. Accessed June 28, 2006.
- Miravittles M, Ferrer M, Pont A, et al. Effect of exacerbations on quality of life in patients with chronic obstructive pulmonary disease: a 2 year follow up study. *Thorax* 2004; 59(5):387–395.
- Seemungal TA, Donaldson GC, Bhowmik A, et al. Time course and recovery of exacerbations in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2000; 161(5):1608–1613.
- Bourbeau J, Ford G, Zackon H, et al. Impact on patient's health status following early identification of a COPD exacerbation. *Eur Respir J* 2007; 30(5):907–913.
- Burge P, Calverley P, Jones P, et al. Randomised, double blind, placebo controlled study of fluticasone propionate in patients with moderate to severe chronic obstructive pulmonary disease: the ISOLDE trial. *BMJ* 2000; 320(7245):1297–1303.
- Calverley P, Pauwels R, Vestbo J, et al. Combined salmeterol and fluticasone in the treatment of chronic obstructive pulmonary disease: a randomised controlled trial. *Lancet* 2003; 361(9356): 449–456.
- Wedzicha JA, Seemungal TA. COPD exacerbations: defining their cause and prevention. *Lancet* 2007; 370(9589):786–796.
- Wilkinson TM, Donaldson GC, Hurst JR, et al. Early therapy improves outcomes of exacerbations of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2004; 169(12): 1298–1303.
- Nici L, Donner C, Wouters E, et al. American Thoracic Society/European Respiratory Society statement on pulmonary rehabilitation. *Am J Respir Crit Care Med* 2006; 173(12):1390–1413.
- O'Donnell DE, Aaron J, Bourbeau J, et al. Canadian Thoracic Society recommendations for management of chronic obstructive pulmonary disease - 2007 update. *Can Respir J* 2007; 14(suppl B):5B–32B.
- Scullion JE. NICE guidelines: the management, treatment and care of COPD. *Br J Nurs* 2004; 13(18):1100–1103.
- Effing T, Monnickhof E, van der Valk P, et al. Self-management education for patients with chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2007; (4):CD002990.
- Bourbeau J, Nault D, Dang-Tan T. Self-management and behaviour modification in COPD. *Patient Educ Couns* 2004; 52(3):271–277.
- Bourbeau J, Nault D. Self-management strategies in chronic obstructive pulmonary disease. *Clin Chest Med* 2007; 28(3):617–628.
- Mazzuca S. Does patient education in chronic disease have therapeutic value? *J Chronic Dis* 1982; 35(7):521–529.
- Bandura A. The assessment and predictive generality of self-percepts of efficacy. *J Behav Ther Exp Psychiatry* 1982; 13(3):195–199.
- Atkins C, Kaplan R, Timms R, et al. Behavioral exercise programs in the management of chronic obstructive pulmonary disease. *J Consult Clin Psychol* 1984; 32:591–603.
- Kaplan RM, Ries AL, Prewitt LM, et al. Self-efficacy expectations predict survival for patients with chronic obstructive pulmonary disease. *Health Psychol* 1994; 13(4):366–368.
- Nault D, Dagenais J, Perreault V, et al. Qualitative evaluation of a disease specific self-management program "Living well with COPD". *Eur Resp J* 2000; 16:317S.
- Wagner EH. Chronic disease management: what will it take to improve care for chronic illness? *Eff Clin Pract* 1998; 1(1):2–4.
- Adams SG, Smith PK, Allan PF, et al. Systematic review of the chronic care model in chronic obstructive pulmonary disease prevention and management. *Arch Intern Med* 2007; 167(6):551–561.
- Piette JD, Weinberger M, Kraemer FB, et al. Impact of automated calls with nurse follow-up on diabetes treatment outcomes in a Department of Veterans Affairs Health Care System: a randomized controlled trial. *Diabetes Care* 2001; 24(2):202–208.
- Simon GE, Von Korff M, Rutter C, et al. Randomised trial of monitoring, feedback, and management of care by telephone to improve treatment of depression in primary care. *BMJ* 2000;320(7234):550–554.
- Weingarten SR, Henning JM, Badamgarav E, et al. Interventions used in disease management programmes for patients with chronic illness-which ones work? Meta-analysis of published reports. *BMJ* 2002; 325(7370):925–928.
- Wagner EH. The role of patient care teams in chronic disease management. *BMJ* 2000; 320 (7234):569–572.
- Zwarenstein M, Stephenson B, Johnson L. Case management: effects on professional practice and health care outcomes. *Cochrane Database Syst Rev* 2000; 4:CD002797.
- Taylor SJ, Candy B, Bryar RM, et al. Effectiveness of innovations in nurse led chronic disease management for patients with chronic obstructive pulmonary disease: systematic review of evidence. *BMJ* 2005; 331(7515):485–488.
- Bourbeau J, Julien M, Maltais F, et al. Reduction of hospital utilization in patients with chronic obstructive pulmonary disease: a disease-specific self-management intervention. *Arch Intern Med* 2003; 163(5):585–591.
- Gadoury MA, Schwartzman K, Rouleau M, et al. Self-management reduces both short- and longterm hospitalisation in COPD. *Eur Respir J* 2005; 26(5):853–857.
- Rea H, McAuley S, Stewart A, et al. A chronic disease management programme can reduce days in hospital for patients with chronic obstructive pulmonary disease. *Intern Med J* 2004; 34(11):608–614.
- Casas A, Troosters T, Garcia-Aymerich J, et al. Integrated care prevents hospitalisations for exacerbations in COPD patients. *Eur Respir J* 2006; 28(1):123–130.
- Garcia-Aymerich J, Lange P, Benet M, et al. Regular physical activity modifies smoking-related lung function decline and reduces risk of chronic obstructive pulmonary disease: a populationbased cohort study. *Am J Respir Crit Care Med* 2007; 175(5):458–463.
- Coultas D, Frederick J, Barnett B, et al. A randomized trial of two types of nurse-assisted home care for patients with COPD. *Chest* 2005; 128(4):2017–2024.
- Monnickhof E, van der Valk P, van der Palen J, et al. Effects of a comprehensive selfmanagement programme in patients with chronic obstructive pulmonary disease. *Eur Respir J* 2003; 22(5):815–820.
- Ley P. Communicating with patients [magazine article]. London: Croom Helm, 1988.
- Morris LA, Halperin JA. Effects of written drug information on patient knowledge and compliance: a literature review. *Am J Public Health* 1979; 69(1):47–52.
- Bourbeau J, Collet JP, Schwartzman K, et al. Economic benefits of self-management education in COPD. *Chest* 2006; 130:1704–1711.
- Bourbeau J, Maltais F, Julien M, et al. Predictors of high utilization of health care services in patients with chronic obstructive pulmonary disease. Abstract. *Can Respir J* 2003;10(4):207
- Gallefoss F, Bakke PS, Rsgaard PK. Quality of life assessment after patient education in a randomized controlled study on asthma and chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1999; 159(3):812–817.
- Kessler R, Stahl E, Vogelmeier C, et al. Patient understanding, detection, and experience of COPD exacerbations: an observational, interview-based study. *Chest* 2006; 130(1):133–142.
- Langsetmo L, Platt RW, Ernst P, et al. Under-reporting exacerbation of chronic obstructive pulmonary disease in a longitudinal cohort. *Am J Respir Crit Care Med* 2008; 177(4):396–401.
- Turnock AC, Walters EH, Walters JA, et al. Action plans for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2005; 4:CD005074.
- Sedeno MF, Nault D, Hamd DH, et al. A written action plan for early treatment of COPD exacerbations: an important component to the reduction of hospitalizations. *Proc Am Thorac Soc* 2006; 3:A603.
- Dowson CA, Town GI, Frampton C, et al. Psychopathology and illness beliefs influence COPD self-management. *J Psychosom Res* 2004; 56(3):333–340.
- Living Well With COPD. Individual Reference Guide: Integrating a Plan of Action for life; October 20, 2006. Available at: www.livingwellwithcopd.com (password: copd).



**Comprehensive self-management
and routine monitoring in COPD patients in
general practice: randomised controlled trial**

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Abstract

Objective

To assess the long-term effects of two different modes of COPD disease management, i.e. comprehensive self-management and routine monitoring, on quality of life (primary objective), frequency and patients' management of exacerbations, and self-efficacy (secondary objectives) in COPD patients in general practice.

Design

24-month, multicentre, investigator-blinded, three-arm, pragmatic, randomised controlled trial.

Setting

15 general practices in the eastern part of the Netherlands.

Participants

Patients with COPD confirmed by spirometry and treated in general practice. Patients with very severe COPD or treated by a respiratory physician were excluded.

Interventions

Participants were randomly allocated to (i) a comprehensive self-management programme as an adjunct to usual care consisting of 4 tailored sessions with ongoing telephonic support by a practice nurse, (ii) routine monitoring as an adjunct to usual care consisting of 2 to 4 structured consultations per year with a practice nurse, or (iii) usual care alone, i.e., contacts with the general practitioner at patients' own initiative. We used a modified version of the self-management programme *Living Well with COPD*. Routine monitoring consultations were based on national COPD guidelines at the time of study.

Outcome measures

Primary outcome was the change in COPD-specific quality of life at 24 months as measured with the Chronic Respiratory Questionnaire total score. Secondary outcomes were Chronic Respiratory Questionnaire domain scores, frequency and patients' management of exacerbations measured with the Nijmegen Telephonic Exacerbation Assessment System, and self-efficacy measured with the COPD Self-efficacy scale. Measurements of quality of life and self-efficacy were at baseline, 6, 12, 18, and 24 months. Measurements of exacerbation rates and management were once every two weeks.

Results

165 patients were allocated to self-management (n=55), routine monitoring (n=55), or usual care alone (n=55). At 24 months, adjusted treatment differences between the three groups in mean Chronic Respiratory Questionnaire total score were not significant. Secondary outcomes did not differ, except for exacerbation management. Compared with usual care, more exacerbations in the self-management group

were managed with bronchodilators and with prednisolone and/or antibiotics; odds ratio 2.81 (95% CI: 1.16 to 6.82) and 3.98 (95% CI: 1.10 to 15.58), respectively.

Conclusions

Comprehensive self-management or routine monitoring did not show long-term benefits on quality of life or self-efficacy over usual care alone in COPD patients in general practice. Patients in the self-management group seemed more capable of appropriately managing exacerbations than in the usual care group.

Trial registration

Clinical trials NCT 00128765

What this paper adds:

What is already known on this subject:

- There is a need for well-studied and proven effective management strategies to face the burden of COPD, particularly in general practice;
- The effects of routine monitoring by COPD guidelines seem to be doubtful;
- Comprehensive self-management programmes have shown benefits, but the effects on COPD patients in general practice are inconclusive.

What this study adds:

- Comprehensive self-management or routine monitoring did not show long-term benefits on quality of life or self-efficacy in COPD patients in general practice;
- Patients in the self-management group seemed more capable of appropriately managing exacerbations than in the usual care group in terms of increasing the use of bronchodilators (46.5% vs 26.5% exacerbations, respectively) and initiating prednisolone and/or antibiotics (15.5% vs 4.9% exacerbations, respectively).

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a slowly progressive lung disease characterized by deterioration of lung function and quality of life and periods of acute exacerbations. Its substantial prevalence - one in 59 people in England were recorded with physician-diagnosed COPD in 2005¹ - and its huge social and economic impact make COPD a major health problem.² Most patients with COPD suffer from mild to moderate disease and are treated in general practice.³ To face the burden of COPD, well-studied and proven effective management strategies are essential, particularly in primary care.

According to current COPD guidelines, symptoms and airflow obstruction should be monitored regularly to modify therapy and to identify complications early.^{2,3} Routine monitoring should contribute to achieving COPD management goals, i.e., to delay disease progression and to alleviate its manifestations.⁴ The

responsibility of this management strategy is largely with the healthcare professional who relies on protocols and acts as expert. The effects of monitoring routines on clinical outcomes such as health status seem to be doubtful.⁴ Besides, it has been questioned whether care should be based on uniform routine consultations or should be more tailored to individual patient needs with a shared responsibility between physician and patient.⁵

Comprehensive self-management programmes focus on the needs of the individual patient. These programmes are based on the presumption that effective behaviour modification can only be attained if patient's self-efficacy has been improved.⁶ Patients who have enough confidence in their ability to successfully respond to certain events, such as in time of an exacerbation, can more easily modify and maintain the desired behaviour. The behaviour modification should ultimately result in improved clinical outcomes.⁷ COPD self-management programmes have shown positive effects on patients' quality of life and healthcare use in secondary care settings, but the benefits in general practice are still inconclusive.^{8,9}

Our primary objective was to assess the long-term effects of two different modes of COPD disease management, i.e., comprehensive self-management and routine monitoring, on quality of life in COPD patients in general practice. As secondary objectives we assessed the effects on frequency and patients' management of exacerbations, and self-efficacy.

Methods

Study design

We performed a 24-month, multicentre, investigator blinded, three-arm, parallel-group, randomised controlled trial. After having provided signed informed consent participating COPD patients were randomly allocated to (i) comprehensive self-management (SM) as an adjunct to usual care, (ii) routine monitoring (RM) through scheduled periodic monitoring visits as an adjunct to usual care, or (iii) usual care alone (UC). The study was approved by the Medical Ethics Committee of the Radboud University Nijmegen Medical Centre (number 2004/249).

Setting and participants

15 general practices in the Netherlands (Nijmegen region) recruited patients between June 2004 and September 2006. The practices invited patients for a study eligibility assessment following a standardised procedure in which they started inviting patients based on a list of all patients who (according to the diagnostic codes in their electronic medical record system) had been diagnosed with COPD.

The order in which the patients appeared on the list was randomised by the investigators. The assessment consisted of pre- and postbronchodilator spirometry¹⁰ and collecting data on sociodemographic characteristics, smoking habits, current co-morbid conditions, and current use of respiratory medication.

Patients were eligible for the study if they were aged ≥ 35 years and post-bronchodilator FEV1/FVC was < 0.70 . Exclusion criteria were postbronchodilator FEV1 < 30 % predicted; treatment by a respiratory physician; severe co-morbid conditions with a reduced life expectancy; unable to communicate in the Dutch language; and objections to one or more of the disease management modes in the study.

Randomisation and interventions

Participants were randomised using a computer-generated two-block randomisation procedure with stratification on COPD severity (mild or moderate *versus* severe airflow obstruction),² smoking status (current *versus* former smoker), and exacerbation frequency in the previous 24 months (< 2 *versus* ≥ 2 exacerbations). To ensure that the investigators were blinded for individual treatment allocation, practice nurses informed the patients of their allocation. Potential treatment contamination caused by providing self-management, routine monitoring and usual care within the same practice was prevented by using strict protocols and registration forms and by providing the required self-management materials only for the patients randomized to the SM group. At the end of the study we reviewed the registration forms and the patients' electronic medical files.

Patients were randomly allocated to UC, SM, or RM. The UC group reflected the care for COPD patients as provided by most general practices in the Netherlands in 2005. Patients received care from their general practitioner (GP) at their own initiative when they consulted with symptoms aggravation. UC patients did not receive any care from the practice nurse, i.e., were not monitored on a routine base nor received (parts of) a self-management programme.

Patients in the SM group received a translated and modified version of the Canadian self-management programme *Living Well with COPD*.¹¹ The version used in the trial was evaluated by 4 Dutch GPs and 4 patients with mild to moderate COPD who did not participate in the trial. Unlike the original Canadian programme, our final version did not include an exercise programme (differences are displayed in Table A of appendix on bmj.com). The SM programme consisted of paper modules and a written exacerbation action plan. Topics covered in the modules were: COPD disease knowledge; respiratory medication; breathing techniques; managing exacerbations; maintaining a healthy lifestyle; managing stress and anxiety (optional); home exercise (optional). The individualised written exacerbation action plan addressed early recognition of and prompt action in the course of an

exacerbation. Actions included increase of bronchodilator use; initiation of standing prescriptions for prednisolone and/or antibiotics (if applicable); or contacting the practice nurse or GP. The practice nurse of each participating practice acted as case manager and applied the programme to the individual patient in 2 to 4 sessions of approximately 1 hour each, scheduled in 4 to 6 consecutive weeks. The sessions took place in the general practice. The number of sessions depended on the patient's needs, but was at least two. Subsequently, the nurse called each patient six times during the rest of the study period to reinforce self-management skills. The nurse was available for advice during business hours. Prior to the study, all nurses were trained in how to apply the SM programme. In addition, all nurses were observed at least once by a respiratory nurse who was a member of the study group and experienced in the self-management programme. The respiratory nurse also coached the practice nurses using a message board on a secured web-based application during the rest of the follow-up.

For participants in the RM group practice nurses scheduled routine monitoring visits in the general practice, on top of usual care. The contents of the monitoring visits were based on the national and international COPD guidelines at time of study.^{12;13} At each consultation, the practice nurse evaluated the severity of symptoms and limitations, health status, adverse effects of and compliance with respiratory medication, the use of inhaler devices, frequency of exacerbations, and once a year measured weight and lung function. The contents of the routine visits were not tailored to individual patient needs, nor were self-management elements included such as the use of a written exacerbation action plan. Individual monitoring frequency was determined by the GP and depended on the severity of airflow obstruction and level of dyspnoea (Medical Research Council dyspnoea score¹⁴), but was at least once a year with a maximum of 4 times a year.

Outcomes and follow-up

Our primary prespecified outcome was the change in health-related quality of life after 24 months from baseline as measured by the self-administered Chronic Respiratory Questionnaire (CRQ-SA).^{15;16} The CRQ-SA consists of 20 questions on a 7-point Likert scale (a higher score indicating better quality of life) that comprise a total score and 4 domain scores: dyspnoea, mastery, fatigue and emotion. The minimal clinically important difference (MCID) of the CRQ has been established at 0.5 points.¹⁷ Secondary prespecified outcomes were the change in CRQ domain scores, exacerbation frequency and management as recorded with an automated call system, and self-efficacy total and five domain scores (see Table 2) as measured with the COPD Self-efficacy Scale (CSES).¹⁸ To assess short-term effects of the interventions differences in CRQ and CSES total and domain scores at 6 months were analysed.

All participants visited the pulmonary function laboratory of the Radboud University Nijmegen Medical Centre at baseline, 12 months, and 24 months. At 6 months and 18 months patients were visited at home by a trained lung function technician. During all study visits the following data were collected: smoking habits, respiratory medication, spirometry,¹⁰ health-related quality of life, and self-efficacy. The data collected were not provided to the practices.

Frequency and patients' management of exacerbations was assessed with the Nijmegen Telephonic Exacerbation Assessment System (TEXAS).¹⁹ Patients were called once every two weeks on the day and time of their preference. Patients answered (yes or no) to an automated voice questions on changes in respiratory symptoms and exacerbation management, i.e. increase of bronchodilator use, initiation of oral prednisolone and/or antibiotics, and unscheduled healthcare use in the two weeks prior to the call. TEXAS was not part of any intervention and did not alert the patient when an exacerbation was imminent. The validity of TEXAS as a research tool has been demonstrated previously.¹⁹ Exacerbations were defined as a change for ≥ 2 consecutive days in either ≥ 2 major symptoms (dyspnoea, sputum purulence, sputum amount) or any 1 major symptom plus any ≥ 1 minor symptoms (colds, wheeze, sore throat, cough).^{20;21}

Sample size calculation and statistical analyses

Sample size calculation using analysis of variance (ANOVA) showed that 55 patients per treatment arm were needed for 80% power ($\alpha=0.05$, two-sided) to detect a minimal clinically important difference (MCID) in the change of the mean CRQ total score of 0.5 points at 24 months with a standard deviation (SD) of 0.8, a mean CRQ total score of 4.8 under the null hypothesis²² and an anticipated dropout rate of 25%. Our primary analysis was based on the intention-to-treat principle and consisted of all available data of all participants. We compared SM with UC and RM with UC. We did not impute any missing data.

Baseline characteristics are presented as number (%), mean (SD) or median (interquartile range). Because of repeated measurements within patients, we performed generalized estimating equations (GEE) analyses with a compound symmetry structure and including the data at all time points (including baseline) to analyze differences within and between groups for the outcomes CRQ total and domain scores and CSES total and domain scores. Only the changes at 6 months (short-term effects) and 24 months (long-term effects) are presented. We used a generalized estimating equations (GEE) logistic regression model with a compound symmetry to estimate differences in clinically important improvements ($\text{MCID} \geq 0.5$) of CRQ total scores between treatment arms. We counted the number of exacerbations recorded by TEXAS. A new exacerbation was distinguished from a previous one if it was preceded by two weeks in which symptoms had not worsened.

Exacerbation rates were expressed as number of exacerbations per patient per year and were compared using weighted rate ratios.²³ Statistical significance was tested using a negative binomial regression analysis with the patient as unit of analysis.²⁴ Differences in exacerbation management were estimated using generalized estimating equations (GEE) logistic regression models with a compound symmetry and exacerbation as unit of analysis. To all models we added sex, age, education level, long-acting bronchodilator use, and inhaled corticosteroid use as covariates. Analyses were done with the statistical package SAS version 9.2 for Windows (SAS Institute Inc., Cary, USA, 1999-2001).

Results

Recruitment and patient characteristics

Patient flow is presented in Figure 1. Of the 748 patients who were considered to have COPD by their GP, 326 (43.6%) did not meet our inclusion criterion of post bronchodilator FEV1/FVC < 0.70. No differences were observed between eligible patients who declined to participate (n=120) and those who were randomized (n=165) regarding age (66.8 vs 65.1 years, p=0.15), sex (60.6% vs 62.9% males, p=0.65), and post bronchodilator FEV1 as % predicted (69.8% vs 67.9%, p=0.38). Almost 16% (n=26) of the patients dropped out during follow-up. Baseline characteristics between drop-outs and those who completed follow-up did not differ. Table 1 shows that at study inclusion patient characteristics were well balanced between the three study groups, except for sex. Overall, more than half of the patients were male, most patients had mild to moderate airflow obstruction, and a median of 1.0 exacerbation was reported to the GP in the two years prior to the study.

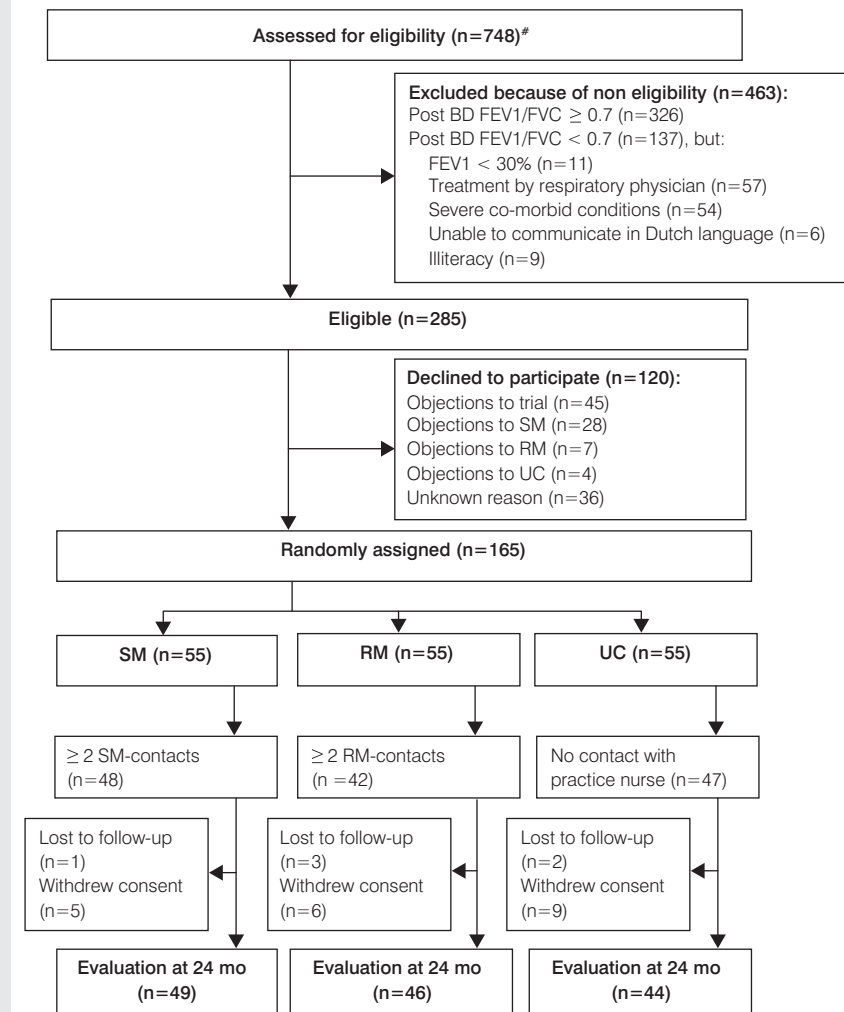
Primary outcome

Figure 2 displays the changes in COPD-specific quality of life (CRQ total score) for SM, RM, and UC. At 24 months, the mean treatment differences between SM and UC and between RM and UC for COPD-specific quality of life (CRQ scores) were not statistically significant (Table 2). More patients in the RM group showed a clinically important improvement compared to the UC group (28.3% vs 18.2%, respectively) (Figure 3), but this difference was not statistically significant (adjusted odds ratio 1.44, 95% CI 0.61 to 3.38).

Secondary outcomes

CRQ domain scores - Changes at 24 months in the CRQ domain scores were not statistically significant (Table 2), except for the dyspnoea domain which showed improvement in the RM group compared to the UC group.

Figure 1 Study flow diagram



* Study eligibility was assessed in general practice by measuring pre- and postbronchodilator lung function (10) and collecting data on sociodemographic characteristics, smoking habits, current medical conditions, and current use of respiratory medication.

Abbreviations: SM = self-management; RM = routine monitoring; UC = usual care

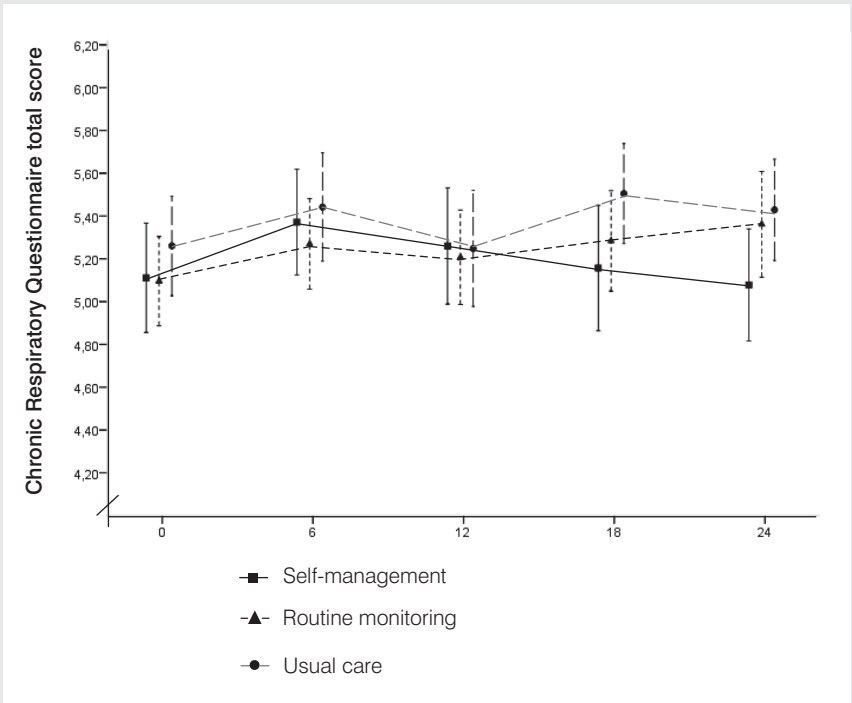
Table 1 Patient characteristics at study inclusion

	SM (n=55)	RM (n=55)	UC (n=55)
Mean age, yr (SD)	65.5 (11.5)	65.8 (8.3)	63.5 (10.3)
Male, n (%)	37 (67.3)	42 (76.4)	28 (50.9)
Median COPD duration, yr (IQR)	7.0 (3.8-13.0)	6.0 (3.0-11.0)	8.0 (4.0-13.0)
Low education level, n (%)	30 (54.5)	35 (63.6)	27 (49.1)
Current smoker, n (%)	16 (29.1)	15 (27.3)	18 (32.7)
Post BD FEV ₁ /FVC < LLN	43 (78.2)	42 (76.4)	38 (69.1)
Mean post BD FEV ₁ , % predicted (SD)	66.3 (16.5)	62.9 (14.4)	67.0 (18.0)
GP previous diagnosed exacerbations [#] , number (IQR)	1.0 (0-2.0)	1.0 (0-2.0)	0.5 (0-2.0)
Mean MRC Dyspnoea Score, (SD)	2.02 (0.94)	1.87 (0.72)	1.73 (0.76)
Respiratory medication, n (%)			
No medication	11 (20.0)	16 (29.1)	19 (39.6)
Long-acting bronchodilators	29 (52.7)	14 (25.5)	10 (20.8)
Inhaled corticosteroids	35 (63.6)	21 (38.2)	17 (30.9)
Relevant comorbidities, n (%)			
Depression or anxiety	4 (7.3)	2 (3.6)	2 (3.6)
Heart failure	7 (12.7)	7 (12.7)	4 (7.2)
Cancer	4 (7.3)	3 (5.5)	1 (1.8)

Abbreviations: SM = self-management; RM = routine monitoring; UC = usual care; post BD = post-bronchodilator; LLN = lower limit of normal; FEV₁ = forced expiratory volume in 1 second; GP = general practitioner; SD = standard deviation; IQR = interquartile range; MRC = Medical Research Council.

[#] Unscheduled contacts with the GP for a worsening of respiratory symptoms in the previous 24 months.

Exacerbation frequency and management - A total of 829 exacerbations were reported by 153 patients. Exacerbation frequency did not differ between the three groups (Table 3). In the second year of follow-up, more exacerbations in the SM group compared to the UC group were managed by an increase of bronchodilator use (OR 2.81, 95% CI 1.16 to 6.82) and by initiation of prednisolone and/or antibiotics (OR 3.98, 95% CI 1.10 to 15.58). Also, in the second study year, more exacerbations in the SM group compared to the other two groups tended to be reported to the GP and/or nurse (not statistically significant) (table 3).

Figure 2 Changes in unadjusted means of Chronic Respiratory Questionnaire total score during 24 months of follow-up for the self-management, routine monitoring, and usual care groups. Bars indicate 95% CIs

CSES total and domain scores - There were no statistically significant changes or differences in patients' self-efficacy according to the CSES total and domain scores at 24 months (Table 2).

Differences at 6 months - At 6 months, differences in CRQ domain scores and self-efficacy total and domain scores were not statistically significant (Table B in appendix on bmj.com). More patients in the SM group than in the UC group achieved a clinically important improvement in the CRQ total score (32.7% vs 24.4%, respectively) (Figure 3), but this was not statistically significant (adjusted OR 1.33, 95% CI 0.52 to 3.4).

Table 2 Primary and secondary clinical outcomes: within and between group differences at 24 months[#]

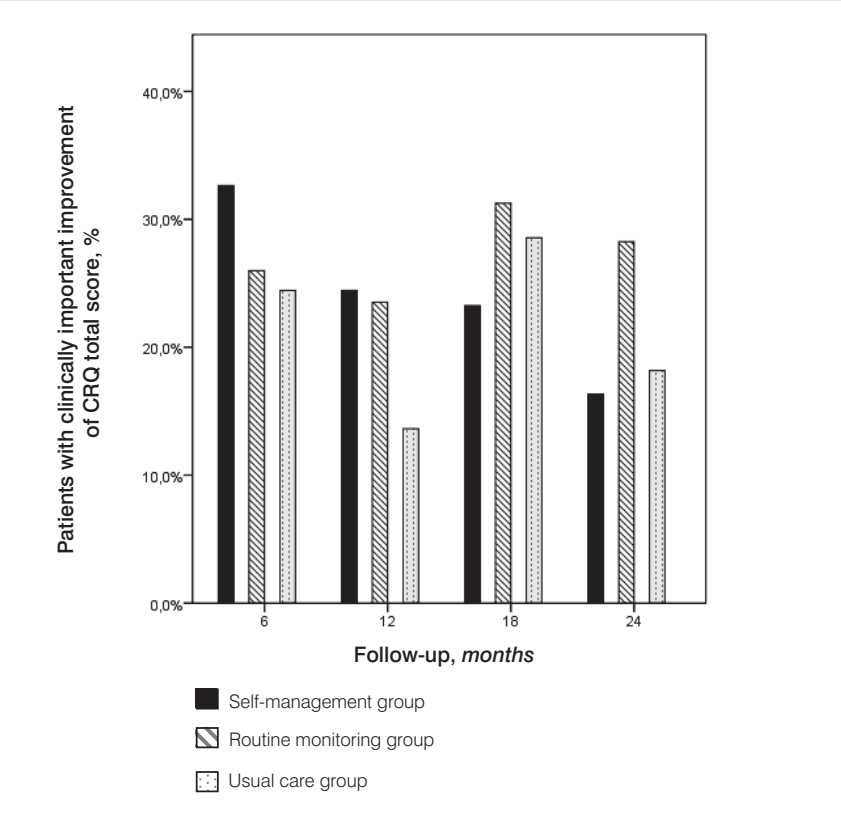
Outcomes	Self-management (n=55)		Routine Monitoring (n=55)		Usual care (n=55)		Treatment difference at 24 months	
Primary	Baseline	Change at 24-mo (95% CI)	Baseline	Change at 24-mo (95% CI)	Baseline	Change at 24-mo (95% CI)	SM vs UC	RM vs UC
CRQ Total	5.11 (0.94)	-0.10 (-0.28 to 0.084)	5.10 (0.77)	0.28 (0.088 to 0.47)	5.26 (0.81)	0.12 (-0.042 to 0.42)	-0.22 (-0.49 to 0.042)	0.16 (-0.11 to 0.42)
Secondary								
CRQ Emotions	5.13 (1.02)	0.0026 (-0.24 to 0.24)	5.18 (0.91)	0.34 (0.088 to 0.59)	5.2 (1.08)	0.31 (0.062 to 0.56)	-0.31 (-0.66 to 0.039)	0.027 (-0.33 to 0.38)
CRQ Mastery	4.75 (0.89)	-0.13 (-0.37 to 0.10)	4.85 (0.77)	-0.017 (-0.26 to 0.23)	4.91 (0.65)	0.071 (-0.17 to 0.32)	-0.20 (-0.55 to 0.14)	-0.088 (-0.44 to 0.26)
CRQ Fatigue	4.79 (1.34)	-0.18 (-0.49 to 0.13)	4.75 (1.18)	0.34 (0.019 to 0.65)	5.04 (1.18)	-0.007 (-0.32 to 0.31)	-0.17 (-0.62 to 0.27)	0.34 (-0.11 to 0.79)
CRQ Dyspnoea	5.68 (1.21)	-0.16 (-0.42 to 0.11)	5.47 (1.29)	0.40 (0.13 to 0.67)	5.82 (1.08)	0.063 (-0.26 to 0.28)	-0.16 (-0.54 to 0.21)	0.40[†] (0.014 to 0.78)
CSES Total	3.53 (1.0)	-0.15 (-0.47 to 0.18)	3.67 (0.86)	-0.12 (-0.45 to 0.20)	3.6 (0.92)	0.025 (-0.31 to 0.36)	-0.17 (-0.64 to 0.30)	-0.15 (-0.62 to 0.32)
CSES Negative affect	3.6 (0.92)	-0.27 (-0.57 to 0.025)	3.51 (1.42)	-0.091 (-0.39 to 0.20)	3.55 (0.84)	-0.22 (-0.53 to 0.09)	-0.053 (-0.48 to 0.38)	0.13 (-0.30 to 0.56)
CSES Emotional arousal	3.67 (0.86)	-0.24 (-0.56 to 0.067)	3.75 (0.8)	-0.24 (-0.55 to 0.07)	3.69 (0.82)	-0.15 (-0.47 to 0.17)	-0.094 (-0.54 to 0.36)	-0.091 (-0.54 to 0.36)
CSES Physical exertion	3.01 (1.11)	-0.053 (-0.36 to 0.26)	3.03 (1.01)	0.16 (-0.15 to 0.47)	2.93 (0.84)	0.12 (-0.20 to 0.45)	-0.17 (-0.62 to 0.27)	0.038 (-0.41 to 0.48)
CSES Weather/ Environment	3.26 (1.0)	-0.18 (-0.49 to 0.12)	3.36 (0.79)	-0.079 (-0.39 to 0.23)	3.26 (0.9)	0.13 (-0.19 to 0.45)	-0.32 (-0.76 to 0.13)	-0.21 (-0.65 to 0.23)
CSES Behavioural risk factors	3.34 (1.02)	-0.17 (-0.49 to 0.15)	3.35 (0.91)	0.019 (-0.30 to 0.34)	3.47 (0.92)	-0.084 (-0.42 to 0.25)	-0.086 (-0.55 to 0.38)	0.10 (-0.36 to 0.57)

Abbreviations: CI = confidence interval; CRQ = Chronic Respiratory Questionnaire; CSES = COPD Self-Efficacy Scale

[#] generalized estimating equations (GEE) analysis with compound symmetry structure and covariates sex, age, education level, long-acting bronchodilator use, and inhaled corticosteroid use, and including data at all time points.

[†] p-value = 0.042

Figure 3 Percentages of patients with clinically important improvements[#] of Chronic Respiratory Questionnaire total score during 24 months of follow-up



[#] Clinically important improvement = ≥ 0.5 improvement in CRQ total score from baseline

Process evaluation

In the SM group, patients received a mean (SD) of 3.4 (1.5) sessions with the practice nurse with a mean (SD) duration of 50.1 (12.8) minutes per session. Practice nurses had 190 telephone contacts with 44 patients (mean contacts 4.5, SD 1.6; mean duration 15.3, SD 4.5 minutes). Seven (12.7%) patients did not receive any session or telephone contact and 48 (87.3%) received ≥ 2 sessions. In the RM group, patients received a mean (SD) of 3.4 (2.5) nurse consultations with a mean (SD) duration of 27.4 (13.7) minutes per contact. Six (10.9%) patients did not receive

Table 3 Differences in rates and patients' management of exacerbations between self-management, routine monitoring, and usual care group

Exacerbation rate* per patient	Rate Ratio #			
	SM (n=53)	RM (n=55)	UC (n=48)	RM vs UC
Baseline – 12 months	2.83	3.25	2.73	1.10 (0.86 – 1.40)
12 months – 24 months	2.45	2.38	2.17	1.16 (0.81 – 1.67)
Exacerbation management				
Number of exacerbations				
Baseline – 12 months	n=150	n=179	n=131	Odds Ratio †
Increase of BD, %	43.4	36.2	30.7	1.70 (0.81 – 3.54)
Prednisolone and/or AB, %	10.5	12.1	10.2	1.24 (0.43 – 3.57)
Unscheduled medical contact, %	13.4	15.0	13.7	1.09 (0.42 – 2.81)
12 months – 24 months	n=130	n=131	n=104	
Increase of BD, %	46.5	43.0	26.5	2.81 (1.16 – 6.82)
Prednisolone and/or AB, %	15.5	7.0	4.9	3.98 (1.10 – 15.58)
Unscheduled medical contact, %	18.6	9.4	11.8	2.07 (0.60 – 7.15)

Abbreviations: SM = self-management; RM = routine monitoring; UC = usual care; BD = bronchodilator; AB = antibiotics

* measured by automated telephonic exacerbation assessment system

weighted rate ratios were tested for statistical significance using negative binomial regression analyses

† odds ratios were estimated using generalized estimating equations (GEE) logistic regression models with a compound symmetry with sex, age, education level, long-acting bronchodilator use, and inhaled corticosteroid use as covariates

any and 42 (76.4%) received ≥ 2 consultations. In the UC group, 8 (14.5%) patients had 1 or more COPD-related scheduled contacts with the practice nurse and, therefore, deviated from the study protocol.

Discussion

Main findings

At 24 months, neither self-management (SM) nor routine monitoring (RM) showed significant benefits over usual care (UC) alone in terms of disease-specific quality of life, exacerbation frequency, or self-efficacy in patients with COPD in general practice. Compared to UC, patients in the SM group seemed to be more capable of taking appropriate actions to manage their exacerbations, i.e. increasing their bronchodilator use and initiating prednisolone and/or antibiotics (odds ratio 2.81 with 95% CI: 1.16 to 6.82 and odds ratio 3.98 with 95% CI: 1.10 to 15.58, respectively).

Strengths and weaknesses of the study

We used an existing, well-studied (in secondary care) and proven effective self-management programme, *Living Well with COPD*,¹¹ instead of developing and testing a new one. This meets the previous criticism on the use of different self-management programmes resulting in insufficient data for meta-analysis and difficulties in formulating clear recommendations.⁸ Our study has a long follow-up (24 months) which follows the hypothesis that it will take time to change behaviour and gain effects caused by self-management in patients with COPD.²⁵

We should be careful with generalizing our results to general practice as a whole. First, more than 60% of the patients who had COPD according to their GP and had a recruitment assessment were excluded. For the majority of cases this was due to a postbronchodilator FEV1/FVC ≥ 0.70 . This suggests that although treated as patient with COPD, a substantial part of the COPD population in general practice has been misdiagnosed according to current guidelines. The recent awareness that spirometry has been underused in general practice²⁶ might improve its use and diminish the number of misdiagnosed COPD patients. Second, of the 285 eligible patients less than 60% was willing to participate. Although these patients were comparable with patients who declined participation regarding sex, age, and disease severity (FEV1), we do not have information on how representative the trial population was regarding other relevant factors such as baseline quality of life and exacerbation history. Third, almost 16% of the participants dropped out during follow-up. However, baseline characteristics did not differ between drop-outs and those who finished follow-up. Also, we anticipated for a drop-out rate of 25% in our sample size calculation. Drop-out rate was lowest in the SM group which may

suggest that patients in this group were more motivated to adhere to COPD treatment because they were more 'involved' in the long-term management of their disease. There is a risk of treatment contamination caused by providing SM, RM, and UC within the same general practice. Therefore, we used strict protocols and registration forms for the practice nurses to minimize the risk of treatment contamination, and checked practices' compliance with the protocols during and after the study. With a clustered randomised trial design the risk of contamination would have been smaller but on the other hand, cluster randomized trials are more complex to implement and require more participants and practices to obtain equivalent statistical power.²⁷

Interpretation with reference to other studies

To our knowledge, this is the first study that compares two different ways of COPD management in patients in general practice. In the SM group, care was tailored to individual needs and there was a close collaboration between the patient and the healthcare professional. In the RM group, care was based on uniform planned contacts and the healthcare provider (practice nurse) acted as an expert and strictly followed the contents of the COPD monitoring protocol.

RM did not effect quality of life, which confirms the results of a previous trial on the effects of a COPD monitoring routine in general practice.²⁸ We could not confirm the effects of the self-management programme on disease-specific quality of life as previously observed in the Canadian trial.¹¹ There may be several explanations for this. First, our version of the programme was provided at a lower intensity than the original Canadian version, i.e., it had a maximum of 4 individual sessions of 50 minutes each compared to weekly one hour sessions for 7 to 8 weeks.¹¹ Thus, there was less time to spend on motivating patients to change their behaviour. Second, the original Canadian programme also included an exercise programme, which may have been an important element of the programme.²⁹ On the other hand, there is no evidence that an hospital-based extensive exercise programme is effective for COPD patients in primary care and, besides, we used the original modules that addressed the importance of physical activity and exercise at home. Third, there were differences between the study populations, i.e. the Canadian patients had more severe COPD, were managed by respiratory specialists in secondary care and had been hospitalised for an acute exacerbation at least once in the preceding year.¹¹ The mean baseline CRQ total score in our study was high and comparable with other primary care COPD studies.^{28,30} This limits the room for improvement in our primary outcome ('ceiling effect'). It would be interesting to explore whether patients with low baseline quality of life scores had more benefit of the programme. However, the size of our study population limits us to perform meaningful subgroup analyses. In contrast with self-management trials that did show positive effects,^{11,31}

we did not use specialised respiratory nurses, but practice nurses who were – a priori – not familiar with the self-management programme. We noticed a wide heterogeneity among them in COPD education, experiences, and attitude and we believe that – despite our training and coaching – individual differences may have influenced the ability of patients to adapt self-management behaviour.

In the process of self-management, self-efficacy and behaviour change are important factors of the causal chain towards potential health gains.⁷ In both the SM and RM groups patients did not show an improvement of perceived self-efficacy as measured with the CSES.¹⁸ This is in line with a recent study.³² Compared to a secondary care COPD population,³³ baseline levels of CSES total and domain scores in our study were high, indicating a high level of confidence. As with quality of life, this could have limited the room for improvement. In our study, self-management behaviour was reflected by exacerbation management. In contrast with the RM group, patients in the SM group received a tailored written action plan for exacerbation management. Equipping COPD patients with a written action plan has previously shown positive effects on exacerbation duration.³⁴ Our finding that, in the second year of the study, patients in the SM group compared to patients in the UC group showed improved exacerbation management in terms of increasing their bronchodilator use and particularly in terms of initiating prednisolone and/or antibiotics suggests that an individualized action plan and a long time-frame are both needed to establish the effects of COPD self-management programmes. The majority of exacerbations remained unreported to the healthcare professional. This is in line with other studies on exacerbation management.^{35,36} Given the importance of timely management of exacerbations to prevent complications and expedite recovery, we propose that further studies on self-management in general practice should focus on effective exacerbation management as the primary outcome.

Conclusions and recommendations for practice

Patients with COPD who were treated in general practice did not benefit from self-management or routine monitoring over usual care alone, except that patients who were enrolled in the self-management programme seemed to be more capable of appropriately managing exacerbations. It should be noted that the chronic care structure in Dutch general practice has significantly evolved since the start of our study. More attention is now paid to the other chronic care components which increase the chance of self-management success.³⁷ Nowadays, there is a better prepared delivery system with structured collaboration between healthcare professionals, more and better equipped practice nurses, and a continuum of care to enhance self-management behaviour, more decision support from secondary care for the diagnosis and management of COPD, and the development of clinical information systems to support both the professional and the patient. Policymakers

and healthcare professionals should consider this when interpreting the findings of our study.

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Ethical approval:

The study was approved by the Medical Ethics Committee of the Radboud University Nijmegen Medical Centre (number 2004/249).

References

- (1) Simpson CR, Hippisley-Cox J, Sheikh A. Trends in the epidemiology of chronic obstructive pulmonary disease in England: a national study of 51,804 patients. *Br J Gen Pract* 2010;60:277-84.
- (2) Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease. Revised 2011. Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD): Available from URL: <http://www.goldcopd.org>. Last updated December 2011; last accessed February 2012.
- (3) Bellamy D, Bouchard J, Henrichsen S, Johansson G, Langhammer A, Reid J et al. International Primary Care Respiratory Group (IPCRG) guidelines: management of chronic obstructive pulmonary disease (COPD). *Prim Care Respir J* 2006;15:48-57.
- (4) van den Bemt L, Schermer T, Smeele I, Bischoff E, Jacobs A, Grol R et al. Monitoring of patients with COPD: a review of current guidelines' recommendations. *Respir Med* 2008;102:633-41.
- (5) Bodenheimer T, Lorig K, Holman H, Grumbach K. Patient self-management of chronic disease in primary care. *JAMA* 2002;288:2469-75.
- (6) Bandura A. The assessment and predictive generality of self-percepts of efficacy. *J Behav Ther Exp Psychiatry* 1982;13:195-99.
- (7) Bourbeau J, Bischoff E, Sedeno MF. Self-management in prevention and early intervention of exacerbations. In: Wedzicha J, Martinez FJ, eds. *Chronic Obstructive Pulmonary Disease Exacerbations*. 1 ed. New York: Informa Healthcare; 2008: 357-68.
- (8) Effing T, Monnikhof EM, Van der Valk PD, van der Palen J, van Herwaarden CL, Partridge MR et al. Self-management education for patients with chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2007;4:CD002990.
- (9) Cranston JM, Crockett AJ, Moss JR, Pegram RW, Stocks NP. Models of chronic disease management in primary care for patients with mild-to-moderate asthma or COPD: a narrative review. *Med J Aust* 2008;188:S50-S52.
- (10) Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A et al. Standardisation of spirometry. *Eur Respir J* 2005;26:319-38.
- (11) Bourbeau J, Julien M, Maltais F, Rouleau M, Beaupre A, Begin R et al. Reduction of Hospital Utilization in Patients With Chronic Obstructive Pulmonary Disease: A Disease-Specific Self-management Intervention. *Arch Intern Med* 2003;163:585-91.
- (12) Geijer RM, van Schayck CP, van Weel C, Sachs AP, Bottema BJ, Smeele IJ et al. NHG-Standaard COPD: behandelingsrichtlijn. *Huisarts Wet* 2001;44:207-19.
- (13) National Institute for Clinical Excellence (NICE). Chronic obstructive pulmonary disease: national clinical guideline for management of chronic obstructive pulmonary disease in adults in primary and secondary care. *Thorax* 2004;59 (Suppl 1):i1-i232.
- (14) Bestall JC, Paul EA, Garrod R, Garnham R, Jones PW, Wedzicha JA. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax* 1999;54:581-86.
- (15) Puhan MA, Guyatt GH, Goldstein R, Mador J, McKim D, Stahl E et al. Relative responsiveness of the Chronic Respiratory Questionnaire, St. Georges Respiratory Questionnaire and four other health-related quality of life instruments for patients with chronic lung disease. *Respir Med* 2007;101:308-16.
- (16) Schunemann HJ, Goldstein R, Mador MJ, McKim D, Stahl E, Puhan M et al. A randomised trial to evaluate the self-administered standardised chronic respiratory questionnaire. *Eur Respir J* 2005;25:31-40.
- (17) Redelmeier DA, Guyatt GH, Goldstein RS. Assessing the minimal important difference in symptoms: a comparison of two techniques. *J Clin Epidemiol* 1996;49:1215-19.
- (18) Wigal JK, Creer TJ, Kotses H. The COPD Self-Efficacy Scale. *Chest* 1991;99:1193-96.
- (19) Bischoff EW, Boer LW, Molema J, Akkermans R, van Weel C, Vercoulen JH et al. Validity of an automated telephonic system to assess COPD exacerbation rates. *Eur Respir J* 2012;39:1090-6.
- (20) Donaldson GC, Seemungal TA, Bhowmik A, Wedzicha JA. Relationship between exacerbation frequency and lung function decline in chronic obstructive pulmonary disease. *Thorax* 2002;57:847-52.
- (21) Seemungal TA, Donaldson GC, Bhowmik A, Jeffries DJ, Wedzicha JA. Time course and recovery of exacerbations in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2000;161:1608-13.
- (22) Schermer T, Chavannes N, Dekhuijzen R, Wouters E, Muris J, Akkermans R et al. Fluticasone and N-acetylcysteine in primary care patients with COPD or chronic bronchitis. *Respir Med* 2009;103:542-51.
- (23) Suissa S. Statistical treatment of exacerbations in therapeutic trials of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2006;173:842-46.
- (24) Aaron SD, Fergusson D, Marks GB, Suissa S, Vandemheen K, Doucette S et al. Counting, analyzing and reporting exacerbations of COPD in randomized, controlled trials. *Thorax* 2008;63:122-28.
- (25) Bourbeau J, Nault D, Dang-Tan T. Self-management and behaviour modification in COPD. *Patient Educ Couns* 2004;52:271-77.
- (26) Poels PJ, Schermer TR, van Weel C, Calverley PM. Spirometry in chronic obstructive pulmonary disease. *BMJ* 2006;333:870-871.
- (27) Campbell MK, Elbourne DR, Altman DG, CONSORT group. CONSORT statement: extension to cluster randomised trials. *BMJ* 2004;328:702-8.
- (28) van den Bemt L, Schermer T, Smeele I, Boonman-de Winter L, van Boxem TJ, Denis J et al. An expert-supported monitoring system for patients with chronic obstructive pulmonary disease in general practice: results of a cluster randomised controlled trial. *Med J Aust* 2009;191:249-54.
- (29) Lacasse Y, Goldstein R, Lasserson TJ, Martin S. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2006;4:CD003793.
- (30) Schermer T, Chavannes N, Dekhuijzen R, Wouters E, Muris J, Akkermans R et al. Fluticasone and N-acetylcysteine in primary care patients with COPD or chronic bronchitis. *Respir Med* 2009;103:542-51.
- (31) Rice K, Dewan N, Bloomfield H, Grill J, Schult T, Nelson D et al. Disease Management Program for Chronic Obstructive Pulmonary Disease. A Randomized Controlled Trial. *Am J Respir Crit Care Med* 2010;182:890-896.
- (32) Bucknall C, Miller G, Lloyd S, Cleland J, McCluskey S, Cotton M et al. Glasgow supported self-management trial (GSuST) for patients with moderate to severe COPD: randomised controlled trial. *BMJ* 2012;344:e1060.
- (33) Kara M, Asti T. Effect of education on self-efficacy of Turkish patients with chronic obstructive pulmonary disease. *Patient Educ Couns* 2004;55:114-20.
- (34) Bischoff EW, Hamd DH, Sedeno MF, Benedetti A, Schermer TR, Bernard S et al. Effects of written action plan adherence on COPD exacerbation recovery. *Thorax* 2011;66:26-31.
- (35) Langsetmo L, Platt RW, Ernst P, Bourbeau J. Underreporting exacerbation of chronic obstructive pulmonary disease in a longitudinal cohort. *Am J Respir Crit Care Med* 2008;177:396-401.
- (36) Wilkinson TM, Donaldson GC, Hurst JR, Seemungal TA, Wedzicha JA. Early therapy improves outcomes of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2004;169:1298-303.
- (37) Adams SG, Smith PK, Allan PF, Anzueto A, Pugh JA, Cornell JE. Systematic review of the chronic care model in chronic obstructive pulmonary disease. *Arch Intern Med* 2007;167:551-61.

Appendix Chapter 6

Table A Comparison of Dutch *Living Well with COPD* version and the original Canadian *Living Well with COPD* programme

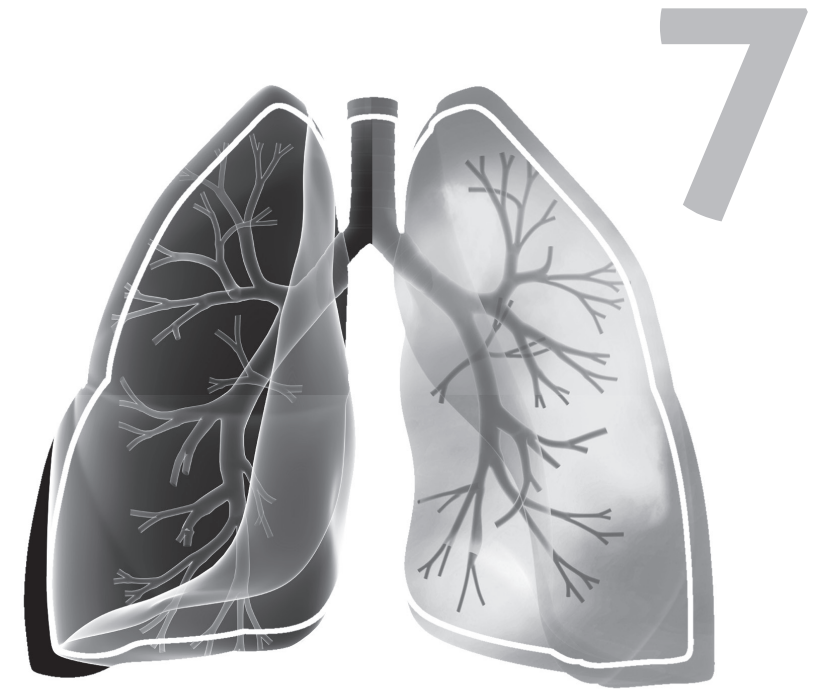
	Dutch <i>Living Well with COPD</i> version	Canadian <i>Living Well with COPD</i> version
Healthcare setting:	General practice	Hospital
Delivery structure:		
Delivery setting	In general practice	At home
Provider	Practice nurses under supervision of GP	Respiratory nurses, respiratory therapists, or physiotherapists under supervision of respiratory physician
Training of provider	<ul style="list-style-type: none"> 8-hour group training addressing contents of the Living Well with COPD programme and motivational interviewing; 1 observation of each practice nurse in daily practice by a respiratory nurse specialized in COPD care; Coaching through message board on secured web-based application during the study. 	<ul style="list-style-type: none"> 9-day group training on every aspect of Living well with COPD, theory and practice of all the techniques and patient teaching; 1 full training day for Exercise module: because most of the healthcare professionals who applied the program were not physiotherapists; Continuous monitoring and support by a nurse specialized in COPD care.
Patient contacts	<ul style="list-style-type: none"> Minimum of 2 to maximum of 4 planned individual sessions of approximately 50 minutes each during 4 to 8 consecutive weeks, followed by; 6 telephone contacts during 24 months follow-up. 	<ul style="list-style-type: none"> 7-8 weeks of planned individual sessions of approximately 1 hour per week, followed by; Weekly telephone calls for 8 weeks, followed by; Monthly telephone calls for the remainder of the 12 month follow-up.
Contents of the programme:		
<i>Educational sessions</i>		
Module "Preventing your symptoms and taking your medications"	Provided to all patients	Provided to all patients.
Module "Keeping a healthy and fulfilling lifestyle"	Provided to all patients	Provided to all patients
Module "Integrating a plan of action into your life"	Provided to all patients	Provided to all patients
Module "Managing your breathing and saving your energy"	Provided to all patients	Provided to all patients
Module: "Managing stress & anxiety"	Provided when appropriate	Provided to all patients
Module: "Integrating an exercise program into your life"	Provided when appropriate	Provided to all patients
Module: "Long-term home oxygen therapy"	Not provided	Provided when appropriate
<i>Exacerbation action plan</i>		
Written paper exacerbation action plan	Standing prescriptions of prednisolone and/or antibiotics depended on the decision of the GP	Standing prescriptions of prednisolone and antibiotics were provided to all patients
<i>Exercise programme</i>		
At home training program with first training under supervision. Patients were encouraged to train 3 times per week for 30 to 45 minutes	Not included	Provided to all patients

Table B Primary and secondary clinical outcomes: within and between group differences at 6 months [#]

Outcomes	Self-management (n=55)		Routine Monitoring (n=55)		Usual care (n=55)		Treatment difference at 6 months	
Primary	Baseline	Change at 6-mo (95% CI)	Baseline	Change at 6-mo (95% CI)	Baseline	Change at 6-mo (95% CI)	SM vs UC	RM vs UC
CRQ Total	5.11 (0.94)	0.25 (0.067 to 0.44)	5.10 (0.77)	0.20 (0.014 to 0.38)	5.26 (0.81)	0.23 (0.042 to 0.42)	0.023 (-0.24 to 0.29)	-0.031 (-0.29 to 0.23)
Secondary								
CRQ Emotions	5.13 (1.02)	0.21 (-0.031 to 0.45)	5.18 (0.91)	0.034 (-0.21 to 0.28)	5.2 (1.08)	0.27 (0.023 to 0.51)	-0.057 (-0.40 to 0.29)	-0.23 (-0.58 to 0.11)
CRQ Mastery	4.75 (0.89)	0.18 (-0.055 to 0.42)	4.85 (0.77)	0.04 (-0.20 to 0.28)	4.91 (0.65)	0.16 (-0.085 to 0.40)	0.025 (-0.31 to 0.36)	-0.12 (-0.46 to 0.22)
CRQ Fatigue	4.79 (1.34)	0.38 (0.073 to 0.69)	4.75 (1.18)	0.40 (0.088 to 0.70)	5.04 (1.18)	0.16 (-0.15 to 0.48)	0.22 (-0.22 to 0.66)	0.23 (-0.21 to 0.67)
CRQ Dyspnea	5.68 (1.21)	0.23 (-0.032 to 0.49)	5.47 (1.29)	0.45 (0.18 to 0.71)	5.82 (1.08)	0.33 (0.062 to 0.59)	-0.098 (-0.47 to 0.28)	0.12 (-0.26 to 0.49)
CSES Total	3.53 (1.0)	-0.034 (-0.34 to 0.28)	3.67 (0.86)	-0.36 (-0.66 to -0.053)	3.6 (0.92)	0.24 (-0.083 to 0.56)	-0.27 (-0.72 to 0.17)	-0.60 (-1.04 to 0.15)
CSES Negative affect	3.6 (0.92)	-0.13 (-0.42 to 0.15)	3.51 (1.42)	-0.29 (-0.57 to -0.0096)	3.55 (0.84)	0.033 (-0.26 to 0.32)	-0.16 (-0.57 to 0.24)	-0.32 (-0.73 to 0.082)
CSES Emotional arousal	3.67 (0.86)	-0.21 (-0.50 to 0.094)	3.75 (0.8)	-0.42 (-0.71 to -0.12)	3.69 (0.82)	0.18 (-0.13 to 0.49)	-0.38 (-0.81 to 0.046)	-0.59 (-1.02 to 0.17)
CSES Physical exertion	3.01 (1.11)	0.062 (-0.23 to 0.36)	3.03 (1.01)	-0.033 (-0.33 to 0.26)	2.93 (0.84)	0.32 (0.014 to 0.62)	-0.26 (-0.68 to 0.17)	-0.35 (-0.77 to 0.071)
CSES Weather/ environment	3.26 (1.0)	-0.0042 (-0.30 to 0.29)	3.36 (0.79)	-0.22 (-0.50 to 0.074)	3.26 (0.9)	0.27 (-0.034 to 0.57)	-0.27 (-0.69 to 0.15)	-0.48 (-0.90 to 0.064)
CSES Behavioral risk factors	3.34 (1.02)	0.025 (-0.29 to 0.34)	3.35 (0.91)	-0.34 (-0.65 to -0.036)	3.47 (0.92)	0.10 (-0.21 to 0.42)	-0.077 (-0.52 to 0.37)	-0.44 (-0.88 to 0.028)

Abbreviations: CI = confidence interval; CRQ = Chronic Respiratory Questionnaire;
CSES = COPD Self-Efficacy Scale

[#] generalized estimating equations (GEE) analysis with compound symmetry structure and covariates sex, age, education level, long-acting bronchodilator use, and inhaled corticosteroid use, and including data at all time points.



Effects of written action plan adherence on COPD exacerbation recovery

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Abstract

Background

The effects of written action plans on recovery from exacerbations of chronic obstructive pulmonary disease (COPD) have not been well studied. The aims of this study were to assess the effects of adherence to a written action plan on exacerbation recovery time and unscheduled healthcare utilisation and to explore factors associated with action plan adherence.

Methods

This was a 1-year prospective cohort study embedded in a randomised controlled trial. Exacerbation data were recorded for 252 patients with COPD who received a written action plan for prompt treatment of exacerbations with the instructions to initiate standing prescriptions for both antibiotics and prednisone within 3 days of exacerbation onset. Following the instructions was defined as adherence to the action plan.

Results

From the 288 exacerbations reported by 143 patients, start dates of antibiotics or prednisone were provided in 217 exacerbations reported by 119 patients (53.8% male, mean age 65.4 years, post-bronchodilator forced expiratory volume in 1 s (FEV₁) 43.9% predicted). In 40.1% of exacerbations, patients adhered to their written action plan. Adherence reduced exacerbation recovery time with statistical ($p=0.0001$) and clinical (-5.8 days) significance, but did not affect unscheduled healthcare utilisation (OR 0.94, 95% CI 0.49 to 1.83). Factors associated with an increased likelihood of adherence were influenza vaccination, cardiac comorbidity, younger age and lower FEV₁ as percentage predicted.

Conclusions

This study shows that adherence to a written action plan is associated with a reduction in exacerbation recovery time by prompt treatment. Knowing the factors that are associated with proper and prompt utilisation of an action plan permits healthcare professionals to better focus their self-management support on appropriate patients.

Introduction

The increasing burden of chronic obstructive pulmonary disease (COPD) on healthcare systems worldwide is mainly caused by exacerbations.¹ These acute events of sustained worsening of the respiratory condition are common in COPD.² Exacerbations have a considerable effect on patients' health status^{3,4} and contribute to COPD-related costs.⁵ Recovery from exacerbations varies from 7 to 14 days,² and it may take even longer to return to activities of daily living.⁴ Despite the huge impact exacerbations may have, patients often have problems in recognising symptom deterioration⁶ and fail to report exacerbations.^{2,7} This causes a delay in treatment which has been associated with an increased symptom recovery time,² a worsening of health status⁴ and an increased risk of hospitalisation.⁸ Leading respiratory societies emphasise enhancement of patients' awareness of exacerbation symptoms and the importance of early intervention.^{5,9}

Self-management education strategies have been shown to improve exacerbation outcomes, for example, by reducing hospital admissions.^{10,11} Effective self-management programmes include written action plans which enable patients with COPD to recognise symptom deterioration in the event of an exacerbation and to react appropriately by prompt initiation of prednisone and/or antibiotics.^{12,13} In the complex sequence of effects resulting from a self-management intervention, it is important to assess patient-reported outcomes if we want to reduce the burden of COPD exacerbations and to claim the benefit of this intervention. The PERCEIVE study has shown that 45% of patients had to stay in bed or on a couch all day during exacerbations; most importantly, 55% declared that quicker symptom relief was the most desired requirement for treatment.¹⁴ Although the use of action plans has been proposed for early recognition and prompt access to treatment,¹⁵ there is currently no evidence that this strategy will improve patient-reported outcomes such as symptom recovery.¹⁶

In the present study the primary aim was to assess the effects of adherence to a written action plan for prompt treatment of exacerbations with standing prescriptions for antibiotics and prednisone on exacerbation recovery time and unscheduled healthcare utilisation. As a secondary objective, patient and disease characteristics that are associated with an enhancement of written action plan adherence were explored.

Methods

Study design

This study was designed as a prospective cohort study embedded within a 1-year randomised clinical trial^{17,18} (<http://ClinicalTrials.gov> identifier: NCT00169897) which compared the effectiveness of outpatient hospital-based exercise training versus

self-monitored home-based exercise training. The methodology of the randomised clinical trial has been described in detail elsewhere.^{17,18} Before randomisation to 8 weeks of either hospital- or home-based exercise training, patients received 4 weeks of group education with the self-management programme 'Living Well with COPD'. This programme is available at <http://www.livingwellwithcopd.com> (password: copd).¹⁹⁻²¹ The programme included the use of a written action plan that focused on prompt treatment of COPD exacerbations with standing prescriptions for antibiotics and oral prednisone. All patients were instructed to initiate both prednisone and antibiotics within 3 days of a change for at least 24 h in at least two of the following three major symptoms: dyspnoea, sputum volume and sputum colour. In each exercise training group, patients were followed by a trained respiratory nurse or respiratory therapist acting as a case manager. The case manager contacted patients every 2 months to reinforce mastery of the intended behaviour and was available for given advice during business hours.

Study subjects

Between 1 January 2004 and 31 November 2005, 10 Canadian centres recruited 252 patients who fulfilled the following inclusion criteria: age ≥ 40 years; forced expiratory volume in 1 s (FEV_1) post-bronchodilator $< 70\%$ predicted and ratio of FEV_1 to forced vital capacity (FVC) < 0.70 ; smoking history ≥ 10 pack years; and MRC dyspnoea scale ≥ 2 .

Measurements

Patients recorded their symptoms, medications and use of healthcare services in a diary. Through standardised monthly telephone interviews, independent research assistants evaluated the diaries for the presence of respiratory symptom changes in the previous month. If so, the interviewer recorded in detail the start and end dates of symptom change; start and end dates of prednisone and antibiotics used, if any; contact with the case manager; unscheduled doctor and emergency room visits and hospital admissions. Spirometry was measured at baseline and at 3 and 12 months. The study definition of adherence to the action plan was based on the instructions given to all enrolled patients, that is, the initiation of both prednisone and antibiotics within 3 days of a change for at least 24 h in at least two of the following three major symptoms: dyspnoea, sputum volume and sputum colour. All other actions were considered as non-adherence. We also used an additional definition, namely, the initiation of prednisone and/or antibiotics within 3 days of a change for at least 24 h in at least two of the three major symptoms.

Exacerbations were defined as a change for at least 24 h in at least two of the three major symptoms (dyspnoea, sputum volume and sputum colour).²² Exacerbations were only considered as new events if there was a time difference of at least 14

days between the exacerbation start date and the end date of the previous one. Exacerbation total recovery time was calculated as the time between exacerbation start date (date of reported symptom change) and end date (when symptoms had returned to baseline level). Treated recovery time was calculated as the time between the medication start date and the exacerbation end date.⁸ Treatment delay was calculated as the time between the exacerbation start date and the medication start date. Unscheduled healthcare utilisation was defined as the use of one or more of the following medical services as recorded in the diaries: unscheduled doctor visit, emergency room visit and hospital admission due to COPD exacerbations.

Statistical analysis

Crude associations between the dependent variables exacerbation total recovery time and unscheduled healthcare utilisation and the independent dichotomous variable adherence to the action plan were calculated using simple linear and logistic regression analyses. These associations were then adjusted for the covariates age, sex, post-bronchodilator $FEV_1\%$ predicted, smoking status, exacerbation severity, contacting the case manager, cardiac disease, use of long-acting bronchodilators and inhaled corticosteroids, influenza vaccination, exacerbation sequence during follow-up and randomisation group in the randomised controlled trial. Before entering the models, correlations between variables were tested and highly correlated variables were dropped. Because of the hierarchical structure of our dataset, intraclass correlation coefficients (ICC) adjusted for the covariates were calculated to explore the clustering effect of exacerbations within subjects and subjects within study centres. Although the ICC of both subject (< 0.0001) and study centre (0.017) was low, we used generalised mixed models with exacerbation occurrence as the unit of analysis and subject and study centre as random effects. For the outcome exacerbation total recovery time, we estimated linear mixed models via restricted maximum likelihood (REML) and, for the outcome unscheduled healthcare utilisation, we estimated logistic mixed models via residual pseudo-likelihood (RSPL). Using comparable analyses we also studied the additional definition of action plan adherence and conducted a worst case analysis in which the exacerbations with missing start dates of antibiotics or prednisone ($n=71$) were included by considering their treatment as failure to adherence.

To explore the relationship between patient and exacerbation characteristics and adherence to the action plan, we estimated logistic mixed models via RSPL with action plan adherence as outcome and subject and study centre as random effects. Inclusion of variables was based on hypothesis as previous research on this topic was not available. We first performed univariable analyses to explore individual associations between action plan adherence and the factors age, sex, post bronchodilator $FEV_1\%$ predicted, exacerbation severity, number of emergency

room visits for COPD in the 12 months prior to the study, having an exacerbation action plan prior to the study, contacting the case manager, cardiac disease, depressive symptoms, influenza vaccination, exacerbation sequence during follow-up and randomisation group in the randomised controlled trial. Multivariable analyses were then conducted to explore the effects of all variables together on the dependent variable adherence to the action plan. Backward elimination was used to remove variables with $p > 0.05$.

The statistical package SPSS Version 16.0.2 was used to calculate baseline characteristics and correlation coefficients and for performing simple linear and logistic analyses. All generalised mixed models were performed using SAS Version 9.2. We considered p values < 0.05 as statistically significant.

Results

Patient and exacerbation characteristics

A total of 143 patients (56.7% of the 252 participants in the randomised controlled trial) reported 288 events that met the study definition of exacerbation. Seventy-one (24.7%) of the 288 exacerbations were excluded due to missing start dates of antibiotics or prednisone. Excluded and included exacerbations were similar with regard to exacerbation recovery time ($p = 0.470$), respiratory symptoms ($p = 0.160$) and patients' age ($p = 0.978$), sex ($p = 0.496$) and FEV_1 ($p = 0.141$). The remaining 217 exacerbations were reported by 119 patients. Table 1 shows the baseline characteristics of these 119 patients who were included in the subsequent analyses. Overall, slightly more than half of the patients were male and most of them had moderate to severe airflow obstruction. The majority were prescribed a combination of long-acting bronchodilators and inhaled corticosteroids. Less than half had been prescribed an intervention plan for COPD exacerbations prior to the study, but this was usually provided as verbal instruction and patients were usually not followed by a case manager.

Table 2 shows the characteristics of the 217 exacerbations analysed. The mean (SD) number of exacerbations per patient was 1.8 (1.2). Slightly more than half of the patients reported only one exacerbation. In most exacerbations there was a worsening of all three major symptoms whereas, in $< 10\%$ of the exacerbations, patients reported a combination of sputum increase with sputum colour change without dyspnoea change. The overall mean (SD) exacerbation total recovery time was 14.0 (9.4) days (median 10.0 days (IQR 8.0-17.0)). Five exacerbations had missing data on the use of unscheduled healthcare services. Half of the exacerbations required unscheduled healthcare utilisation of which most required only unscheduled doctor visits. Less than 10% of the exacerbations required emergency room visits followed by hospital admission.

Table 1 Subject characteristics at baseline (n=119)

Characteristic description	Data at baseline
Age, years	65.4 (9.2)
Male	64 (53.8)
Years of education	11.2 (4.0)
Current smoker	23 (19.3)
Pack years	58.8 (39.0 - 67.5)
BMI, kg/m ²	27.2 (5.9)
Post-BD FEV ₁ , L	1.07 (0.32)
Post-BD FEV ₁ , % predicted	43.9 (13.3)
Post-BD FEV ₁ /FVC	0.43 (0.11)
6-min walking distance, meters	339 (284 – 395)
Dyspnea score (MRC)	
2/5	29 (24.6)
3/5	53 (44.9)
4/5	25 (21.2)
5/5	11 (9.3)
ER visits for COPD in previous 12 months	0.65 (1.05)
ICS and LABD	91 (76.5)
Co morbidity	
Depressive symptoms *	32 (29.9)
Cardiac disease #	29 (24.4)
Exacerbation intervention plan prior to study	48 (41.0)
Influenza vaccination	95 (80.5)
Intervention group in RCT *	
Home-based rehabilitation	60 (50.4)
Hospital-based rehabilitation	59 (49.6)

Definition of abbreviations: AP = action plan; BMI = body mass index; Post-BD FEV₁, % predicted = post bronchodilator Forced Expiratory Volume in the first second as percentage of predicted; FEV₁/FVC = ratio of Forced Expiratory Volume in first second and Forced Volume Capacity; MRC = Medical Research Council; ER = emergency room; ICS = inhaled corticosteroid; LABD = long acting bronchodilator.

* Depressive symptoms were measured with the 15-item Geriatric Depression Scale (GDS). Numbers presented include scores suggestive for depression (score ≥ 6 points).

Cardiac disease includes chronic heart failure, angina pectoris, myocardial infarction, and arrhythmia.

* Canadian pulmonary rehabilitation trial (ClinicalTrials.gov identifier: NCT00169897)

Data are expressed as mean (standard deviation) or median (interquartile range) for continuous variables or number (%) for categorical variables.

Table 2 Exacerbation characteristics (n=217)

Characteristic description	Results
Exacerbation frequency (per patient per year)	1.8 (1.2)
Patients with	
1 exacerbation	67 (56.3)
2 exacerbations	24 (20.2)
3 exacerbations	17 (14.3)
4 or more exacerbations	11 (9.2)
Exacerbation symptoms:	
Increase in dyspnea and sputum, change in sputum color	136 (32.7)
Increase in dyspnea and sputum	30 (13.8)
Increase in sputum and change in sputum color	19 (8.8)
Increase in dyspnea and change in sputum color	32 (14.7)
Exacerbation total recovery time, days	14.0 (9.4)
Treated recovery time, days	11.6 (7.9)
Exacerbations with unscheduled healthcare utilization*:	
Total	107 (50.5)
Unscheduled doctor visit	70 (33.0)
ER	20 (9.4)
ER + Hospital admission	17 (8.0)

Definition of abbreviations: ER = emergency room
Data are expressed as mean (standard deviation) for continuous variables or number (%) for categorical variables.
* Five exacerbations were excluded due to missing data concerning the use of unscheduled healthcare services.

Action plan adherence, exacerbation recovery time and unscheduled healthcare utilisation

Overall, the median treatment delay was 1.0 day (IQR 0.0-3.5). In 141 exacerbations (65.0%) patients initiated both antibiotics *and* prednisone, whereas in only 8 exacerbations (3.7%) patients failed to start any oral medication. Patients were adherent to their action plan in 87 (40.1%) of the reported exacerbations. Exacerbations in which patients were non-adherent consisted of events treated with only prednisone (n=11, 8.5%), only antibiotics (n=61, 46.9%), both but not within the 3-day time delay (n=50, 38.5%) and those not treated with any oral medication (n=8, 6.2%).

Using the additional definition of action plan adherence (initiation of prednisone and/or antibiotics within 3 days time delay) resulted in 133 exacerbations (61.3%) in which patients were adherent. Of these exacerbations, 34 were treated with only antibiotics, 5 with only prednisone and 94 with both.

Table 3 shows that exacerbations in which patients were adherent had a faster recovery (-5.08 days) to baseline than exacerbations in which patients were non-adherent (p=0.0001). The effect on exacerbation total recovery time remained significant when analysing only patients' first and last exacerbations (-7.09 days, 95% CI -10.56 to -3.63, p=0.0001 and -4.99 days, 95% CI -9.03 to -0.95, p=0.016, respectively; data not shown). When analysing the additional definition of action plan adherence (initiation of prednisone and/or antibiotics within 3 days time delay), the effect on total recovery time increased; the increase was both clinically and statistically significant (7.43 days, p=0.0001). Furthermore, when conducting the worst case analysis, the effect remained significant. The difference in treated recovery time between action plan adherence and non-adherence was not statistically significant. There was no difference observed in the use of unscheduled healthcare services between exacerbations in which patients were adherent and non-adherent using the study definition and the additional definition of adherence and when conducting the worst case analysis.

After adjustment for potential confounding factors, the association between adherence to the action plan and exacerbation total recovery time increased to -5.84 days (95% CI -8.44 to -3.23). Also, for the additional definition and in the worst case analysis, the association remained clinically and statistically significant. After adjustment, the differences in treated recovery time between adherence and non-adherence remained not statistically significant. Adjustment did not change the association between adherence and unscheduled healthcare utilisation.

Adherence to the action plan and associated factors

Table 4 shows the relationship between patient and disease characteristics and adherence to the action plan in the multilevel univariable and multivariable analyses. In the univariable analysis, adherence was more likely in exacerbations of patients with cardiac disease and those who received influenza vaccination. Patients with higher FEV₁ were less likely to adhere to their written action plan. When combining all factors in the multivariable analysis, patients receiving influenza vaccination, having cardiac comorbidity, having more severe airflow obstruction and being younger had an increased likelihood of adhering to the action plan. After adjustment for the covariates, exacerbations within patients were slightly more similar to each other than to exacerbations in other patients (ICC=0.125) in terms of action plan adherence. Also, patients within a centre were slightly more similar to each other than to patients in other centres (ICC=0.134) in terms of action plan adherence.

Table 3 Effect of adherence to the written action plan on exacerbation recovery time and unscheduled healthcare utilization

Study definition * (n=217 exacerbations)	Adherence		Crude			Adjusted ‡		
	Yes (n=87)	No (n=130)	B / OR	95% CI	p-value	B / OR	95% CI	p-value
Exacerbation total recovery time, days	10.9 (5.6)	16.0 (10.7)	-5.08	-7.62 to -2.55	0.0001	-5.84	-8.44 to -3.23	0.0001
Treated recovery time, days	10.5 (5.6)	12.3 (9.0)	-1.8	-4.03 to 0.42	0.112	-2.21	-4.58 to 0.16	0.072
Unscheduled healthcare utilization, yes *	42 (49.4)	65 (51.2)	0.93	0.54 to 1.61	0.801	0.94	0.49 to 1.83	0.864
Additional definition § (n=217 exacerbations)	Yes (n=87)	No (n=130)						
Exacerbation total recovery time, days	11.2 (6.8)	18.6 (11.1)	-7.43	-9.91 to -4.96	0.0001	-7.36	-9.85 to -4.87	0.0001
Treated recovery time, days	10.7 (6.7)	13.1 (9.3)	-2.38	-4.66 to 0.1	0.040	-2.04	-4.37 to 0.29	0.090
Unscheduled healthcare utilization, yes *	39 (50.6)	65 (50.0)	0.97	0.67 to 1.72	0.928	0.99	0.52 to 1.96	0.978
Worst case analysis ¶ (n=288 exacerbations)	Yes (n=87)	No (n=201)						
Exacerbation total recovery time, days	10.9 (5.6)	15.0 (10.2)	-4.09	-6.46 to -1.72	0.001	-4.87	-7.31 to -2.43	0.0002
Unscheduled healthcare utilization, yes *	42 (49.4)	109 (55.1)	0.8	0.48 to 1.33	0.384	0.78	0.43 to 1.41	0.412

Definition of abbreviations: B = regression coefficient, i.e. the change in recovery time with adherence; OR = Odds Ratio; CI = Confidence Interval.
* Study definition: Action plan adherence was defined as the initiation of both prednisone and antibiotics within 3 days of exacerbation onset. All other actions were defined as non-adherence. § Additional definition: Adherence was defined as the initiation of prednisone and/or antibiotics within 3 days of exacerbation onset. All other actions were defined as non-adherence. ¶ In the worst case analysis all reported exacerbations were included considering the exacerbations with missing data on the use of antibiotics and/or prednisone as failure to adherence. Adherence was defined as the initiation of prednisone and antibiotics within 3 days of exacerbation onset. Treated recovery time was not calculated as the exacerbations that were added had missing start dates of treatment. * Five exacerbations were excluded due to missing data concerning the use of unscheduled healthcare services. ‡ Adjusted for age, sex, post bronchodilator FEV1 % predicted, smoking status, exacerbation severity, contacting the case manager, cardiac disease, use of LABD and ICS, influenza vaccination, exacerbation sequence during follow-up and randomization group in the RCT.

Table 4 Factors associated with adherence to the action plan#: *univariable* and *multivariable* analyses on 217 exacerbations

Univariable analysis	Categories or units	OR	95% CI
Influenza vaccination	yes vs no	4.83	1.74 to 13.37
Cardiac disease §	yes vs no	2.44	1.08 to 5.52
Exacerbation intervention plan prior to study	yes vs no	1.63	0.75 to 3.54
Post-BD FEV1	each % predicted	0.98	0.96 to 1.00
Age	each year	0.98	0.94 to 1.02
Sex	female vs male	1.28	0.65 to 2.52
Exacerbation sequence	each exacerbation	1.11	0.84 to 1.46
Number of exacerbation symptoms	3 vs 2 symptoms	1.45	0.73 to 2.87
ER COPD visit prior to study	each visit	1.11	0.85 to 1.44
Contacting the case manager	yes vs no	1.19	0.6 to 2.38
Depressive symptoms ¶	yes vs no	0.95	0.85 to 1.07
Pulmonary rehabilitation in RCT *	home vs hospital	1.25	0.63 to 2.48
Multivariable analyses §			
Influenza vaccination	yes vs no	4.82	1.71 to 13.54
Cardiac disease	yes vs no	3.05	1.26 to 7.39
Age	each year	0.96	0.92 to 1.00
Post-BD FEV1	each % predicted	0.98	0.95 to 1.00
Random effects		Estimate	95% CI
Subject		0.47	-0.32 to 1.26
Study centre		0.51	-0.33 to 1.35

Definition of abbreviations: OR = Odds Ratio; CI = Confidence Interval; Post-BD FEV1 = post broncho-dilator Forced Expiratory Volume in the first second.
Adherence to the action plan was defined as the initiation of both prednisone and antibiotics within 3 days of exacerbation onset. All other actions were defined as non-adherence.
§ Cardiac disease includes chronic heart failure, angina pectoris, myocardial infarction, and arrhythmia.
¶ Depressive symptoms were measured with the 15-item Geriatric Depression Scale (GDS). Sum scores (range 0-15) ≥ 6 points are suggestive for depression.
* Canadian pulmonary rehabilitation trial (ClinicalTrials.gov identifier: NCT00169897)
§ After backward elimination with removal of variables with p>0.05

Discussion

Main findings

This study shows that adherence to a written action plan with instructions for prompt and proper treatment of exacerbations is associated with a statistically ($p=0.0001$) and clinically (-5 days) significant reduction in exacerbation total recovery time. The study could not demonstrate a reduction in unscheduled healthcare utilisation. Factors such as receiving influenza vaccination, having a cardiac comorbidity, having more severe airflow obstruction and being younger increased the likelihood of adherence to the action plan.

This is the first study to demonstrate a positive association between the use of a written action plan and exacerbation total recovery time. This is important in view of new data showing that exacerbations are so disabling that patients have expressed that quicker symptom relief was the most desired treatment goal.¹⁴ Wilkinson and colleagues showed that a time delay in exacerbation treatment significantly extended exacerbation recovery time, with 0.42 days per additional day delay.⁸ They instructed patients to report exacerbations to the study team or the healthcare provider. The reported median delay in treatment was 3.7 days (IQR 2.0-5.6). Standing prescriptions as part of an action plan benefits early treatment as patients in the current study initiated medication with a median treatment delay of only 1.0 day (IQR 0.0-3.5). Action plan adherence was also associated with a decrease of 2.2 days in treated recovery time, although this finding did not reach statistical significance. Our study was not sufficiently powered to show such a small difference. Action plan adherence was not associated with a reduction in the use of healthcare services. This is in contrast with recent studies on the use of COPD action plans. Seden and colleagues showed an association between the same written action plan and a reduction in hospital admission and emergency room visits, but included older subjects with a worse disability (6 min walking test and MRC dyspnoea score).²³ In addition, Sridhar et al showed that a written action plan embedded in a care package containing pulmonary rehabilitation and self-management education reduced the need for primary care consultations compared with care as usual after a 2-year follow-up.²⁴

To improve the use of written action plans in daily practice, it is important to understand why patients may fail to adhere to their written action plan. In the present study, despite the training programme at the start and the support by case managers during the 1-year follow-up, in only 40.1% of the exacerbations did patients adhere to the action plan. However, the primary goal of the overall self-management intervention was exercise maintenance after completing a pulmonary rehabilitation programme. The intervention could have been more effective if it focused on the use of an action plan in the event of an exacerbation. Patients with worse disease severity (i.e., lower

lung function or cardiac comorbidity) were more likely to adhere to their action plan. This suggests a tendency among healthier patients to delay their treatment regardless of exacerbation severity. Although adherence to pulmonary medication has been associated with older age,²⁵ the current study showed that adherence to an action plan was associated with younger age. It is possible that adherence to an action plan is higher in younger subjects because of an increased perception by patients of the exacerbation on daily health and activities. Also, patients who received an influenza vaccination were more likely to adhere to their action plan. This may reflect a more favourable patient's belief or a higher quality of communication between the patient and provider. Depression has been shown to inhibit COPD self-management,²⁶ but depressive symptoms were not associated with action plan use in our study. Exacerbation sequence was not associated with action plan adherence. Since many patients experienced only one exacerbation over the 1-year study period, it is not realistic to expect adoption of a new behaviour in all patients. Successful past experiences can enhance self-efficacy, which is a predictor of behavioural change.¹⁹ An observation period of >1 year would better match the time frame in which self-management support objectives can be attained. Furthermore, a longer time course in which behaviour change can happen might result in a more realistic time allowance for longterm outcomes such as hospitalisations.

This study has several limitations. First, it was embedded in a randomised clinical trial that was designed for a different purpose. The results should thus be interpreted with some caution. Second, the written action plan was part of an intervention that consisted of the self-management programme 'Living Well with COPD' and pulmonary rehabilitation. The self-management programme has previously demonstrated a significant reduction in healthcare utilisation and an improvement in health status,²⁰ even after a 2-year follow-up period.²¹ The pulmonary rehabilitation programme home-based as well as hospital-based has recently been shown to improve COPD-specific quality of life.¹⁸ The current study therefore does not allow us to draw any conclusions about the effects of a streamlined written action plan, only the use of an action plan as part of a more comprehensive self-management programme. On the other hand, the action plan was the only part of the intervention programme that specifically focused on exacerbation self-management. Third, 25% of the exacerbations had to be excluded because of missing exacerbation start or end dates and missing information regarding the use of antibiotics or prednisone. Although the excluded exacerbations did not differ from those analysed, this has definitely decreased the power of the study. Fourth, we excluded exacerbations that occurred within 14 days of the previous one and this could have affected the results.²⁷ However, only 3.6% of the exacerbations were excluded for this reason and including them in the analyses did

not change the statistical or clinical significance. Finally, to maximise the power of our study we used data of all exacerbations, thereby increasing the risk of introducing bias by frequent exacerbators. By entering the sequence of exacerbations as a variable in our multivariable regression models, we minimised this risk.

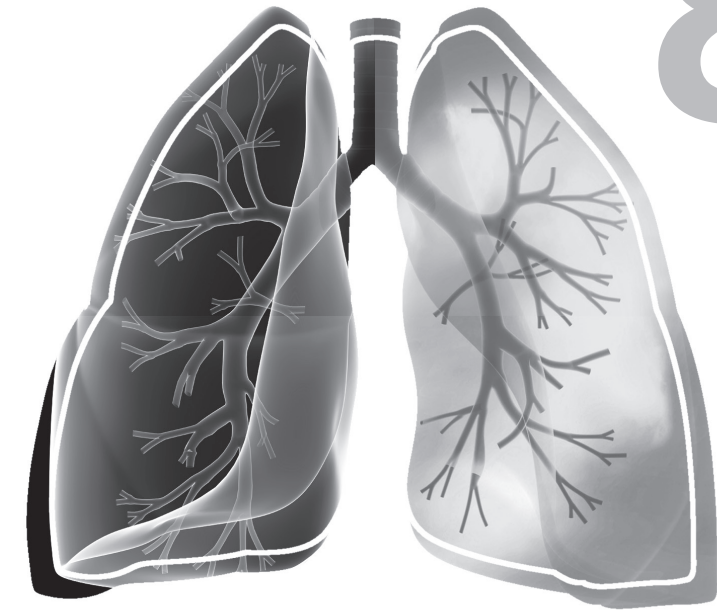
Implications for practice and future research

The results of this study have significant implications for clinical practice. We have shown that a written action plan is associated with a reduction in exacerbation total recovery time providing patients adhere to it. This suggests that action plans deserve a more prominent role in exacerbation management. However, less than half of the exacerbations were treated according to the instructions. Sufficient time and supportive coaching for patients should be allowed to improve the management of exacerbations. Although several factors were found that can be used by healthcare professionals to provide better self-management support, additional research on this topic is needed. Taking into account the negative results of previous studies, action plans should be carefully embedded in well-designed care delivery systems with easy access to care, including continuous reinforcement by case managers. This needs further research if we want a better understanding of what the specific components are, the time frame in which specific behaviour change such as using an action plan in the event of an exacerbation can be attained, and how best to support self-management in COPD.²⁸

References

1. Seemungal TA, Donaldson GC, Paul EA, et al. Effect of exacerbation on quality of life in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1998;157:1418-22.
2. Seemungal TA, Donaldson GC, Bhowmik A, et al. Time course and recovery of exacerbations in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2000;161:1608-13.
3. Miravittles M, Ferrer M, Pont A, et al. Effect of exacerbations on quality of life in patients with chronic obstructive pulmonary disease: a 2 year follow up study. *Thorax* 2004;59:387-95.
4. Bourbeau J, Ford G, Zackon H, et al. Impact on patients' health status following early identification of a COPD exacerbation. *Eur Respir J* 2007;30:1-7.
5. Rabe KF, Hurd S, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med* 2007;176:532-55.
6. Kessler R, Stahl E, Vogelmeier C, et al. Patient understanding, detection, and experience of COPD exacerbations: an observational, interview-based study. *Chest* 2006;130:133-42.
7. Langsetmo L, Platt RW, Ernst P, et al. Under-reporting exacerbations of COPD in longitudinal cohort. *Am J Respir Crit Care Med* 2008;177:396-401.
8. Wilkinson TM, Donaldson GC, Hurst JR, et al. Early therapy improves outcomes of exacerbations of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2004;169:1298-303.
9. Celli BR, MacNee W. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *Eur Respir J* 2004;23:932-46.
10. Effing T, Monnikhof EM, Van der Valk PD, et al. Self-management education for patients with chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2007;(4):CD002990.
11. Taylor SJ, Candy B, Bryar RM, et al. Effectiveness of innovations in nurse led chronic disease management for patients with chronic obstructive pulmonary disease: systematic review of evidence. *BMJ* 2005;331:485.
12. Wood-Baker R, McGlone S, Venn A, et al. Written action plans in chronic obstructive pulmonary disease increase appropriate treatment for acute exacerbations. *Respirology* 2006;11:619-26.
13. McGeoch GR, Willsman KJ, Dowson CA, et al. Self-management plans in the primary care of patients with chronic obstructive pulmonary disease. *Respirology* 2006;11:611-18.
14. Miravittles M, Anzueto A, Legnani D, et al. Patient's perception of exacerbations of COPD: the PERCEIVE study. *Respir Med* 2007;101:453-60.
15. Nici L, Donner C, Wouters E, et al. American Thoracic Society/European Respiratory Society statement on pulmonary rehabilitation. *Am J Respir Crit Care Med* 2006;173:1390-413.
16. Turnock AC, Walter EH, Walters JA, et al. Action plans for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2005;(4):CD005074.
17. Maltais F, Bourbeau J, Lacasse Y, et al. A Canadian, multicentre, randomized clinical trial of home-based pulmonary rehabilitation in chronic obstructive pulmonary disease: rationale and method. *Can Respir J* 2005;12:193-8.
18. Maltais F, Bourbeau J, Shapiro S, et al. Effects of home-based pulmonary rehabilitation in patients with chronic obstructive pulmonary disease. *Ann Intern Med* 2008;149:869e78.
19. Bourbeau J, Nault D. Self-management strategies in chronic obstructive pulmonary disease. *Clin Chest Med* 2007;28:617-28.
20. Bourbeau J, Julien M, Maltais F, et al. Reduction of hospital utilization in patients with chronic obstructive pulmonary disease: a disease-specific self-management intervention. *Arch Intern Med* 2003;163:585-91.
21. Gadoury M-A, Schwartzman K, Rouleau M, et al. Self-management reduces both short- and long-term hospitalisation in COPD. *Eur Respir J* 2005;26:853-7.
22. Anthonisen NR, Manfreda J, Warren CPW, et al. Antibiotic therapy in exacerbations of chronic obstructive pulmonary disease. *Ann Intern Med* 1987;106:196-204.
23. Sedeno MF, Nault D, Hamd DH, et al. A self-management education program including an action plan for acute COPD exacerbations. *COPD* 2009;6:352-8.

24. Sridhar M, Taylor R, Dawson S, et al. A nurse-led intermediate care package in patients who have been hospitalised with an acute exacerbation of chronic obstructive pulmonary disease. *Thorax* 2008;63:194-200.
25. Rand CS, Nides M, Cowles MK, et al. Long-term metered-dose inhaler adherence in a clinical trial. The Lung Health Study Research Group. *Am J Respir Crit Care Med* 1995;152:580-8.
26. Dowson CA, Town GI, Frampton C, et al. Psychopathology and illness beliefs influence COPD self-management. *J Psychosom Res* 2004;56:333-40.
27. Hurst JR, Donaldson GC, Quint JK, et al. Temporal clustering of exacerbations in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2009;179:369-74.
28. Bourbeau J, van der Palen J. Promoting effective self-management programmes to improve COPD. *Eur Respir J* 2009;33:461-3.



General Discussion

The interest of researchers, healthcare professionals, and health policy makers in chronic obstructive pulmonary disease (COPD) and its exacerbations has increased enormously in the last decades. There are two important reasons for this: 1) COPD is predicted to be one of the most common chronic conditions worldwide in the coming years¹; and 2) As COPD cannot be cured, there is an urgent need for disease management strategies that slow disease progression, prevent complications, and diminish the burden on patients and healthcare systems.

The chapters included in this thesis address the impact of COPD and its exacerbations on primary care and the role of COPD self-management as innovative disease management strategy to diminish the impact. These two topics are discussed below in the light of the results described in this thesis and with respect to current literature and future perspectives.

The impact of COPD: a primary care perspective

So far, many studies have reported the growing burden of COPD using various outcomes, such as cost-related outcomes, disability-adjusted life years, and mortality figures.¹ Although relevant from the economic or societal perspective, these figures are less relevant to healthcare professionals in the management of their patients. Information on how the impact of COPD and its exacerbations has actually changed in daily practice is of particular interest for general practitioners (GPs), as most patients with COPD are treated in primary care.² The study described in *Chapter 2* revealed that the overall prevalence of physician-diagnosed COPD has decreased significantly during the last decades in Dutch general practice. This finding, while in line with other prevalence studies,³⁻⁶ is in contrast with the predictions that COPD will be one of the most common chronic conditions in the nearby future, as it suggests a decrease rather than an increase of the impact of COPD on primary care. However, the number of patients that need care is still substantial and literature suggests that the current care for COPD patients in general practice requires improvement.⁷ Besides, when interpreting practice-based prevalence rates, we should also consider the diagnostic process of COPD, under-reporting of its exacerbations and the impact of COPD at patient level.

Misdiagnosis and missed diagnosis of COPD

Chapter 6 revealed that almost 50% of patients who had COPD according to their GP were “misdiagnosed” as they appeared to have a postbronchodilator FEV₁/FVC ≥ 0.70 , and so did not fulfil the current most important criterion of COPD.¹ Similar percentages were also found in other primary care COPD studies.⁷⁻⁹ Until 1997, Dutch GPs followed the concept of Chronic Non-Specific Respiratory Disease

(CNSRD [CARA]), an umbrella term for chronic respiratory diseases, in the diagnosis of COPD and asthma.^{10,11} Since 1997, spirometry has been the most essential test to objectify the airflow limitation that is required for diagnosing COPD and to differentiate COPD from asthma.¹² Recently, the lower limit of normal (LLN) has been proposed to replace the current criterion of post bronchodilator $FEV_1/FVC < 0.70$ to define airflow limitation, as the latter criterion tends to overestimate COPD in the elderly¹³ and underestimate it in younger people.¹⁴ Despite the evolving insights on defining and diagnosing COPD, many patients apparently still carry a diagnosis that has been made many years ago in general practice, but has not been confirmed since then.

Prevalence rates are based on patients in whom the COPD diagnosis has already been established. COPD prevalence in the CMR Nijmegen practices in 2006 was 54 patients per 1000 patients per year (*Chapter 2*). Much higher rates were found in population-based studies with estimates of spirometry-confirmed COPD prevalences between 11.4 and 26.1%.^{15,16} Previously, using data from the DIMCA-programme,¹⁷ Albers *et al.* demonstrated a considerable underrepresentation and underdiagnosis of COPD in general practice.¹⁸ It may be concluded that the CMR Nijmegen registration data, like any other practice-based registration system, also underestimates the true prevalence of COPD. Obviously, the prevalence of COPD known to the GP is only the tip of the iceberg. Undiagnosed patients may have significant impairment in health-related quality of life and activities of daily life.¹⁹ Early detection of patients at high risk in general practice is highly desirable and feasible²⁰ and hastens the start of disease management.

Under-reporting of COPD exacerbations

The trend in COPD exacerbation occurrence rates in the CMR Nijmegen practices showed a gradual decline to 31 exacerbations per 100 COPD patients in 2006 (*Chapter 2*). This means that one COPD patient would have approximately one exacerbation per three years according to the GP medical records. The results described in table 3 of *Chapter 6* confirm this finding, but add some very relevant information: the usual care group showed an exacerbation rate (symptom-based definition) of 2.73 per patient per year of which only approximately 14% (equivalent to approximately one exacerbation every three years) was presented to the GP. Apparently, there is a huge under-reporting of exacerbations in primary care which is much larger than in secondary care where 30%²¹ to 66%²² of exacerbations are reported. Unreported exacerbations may have an impact on quality of life^{21,22} and may increase the risk of complications.²² Early recognition of symptom worsening should be a major objective in primary care COPD management. Strategies that focus on early recognition of exacerbations, such as interventions comprising written exacerbation action plans (*Chapter 7*) are helpful, but should be thoroughly

studied before implemented in daily practice. This requires valid tools, such as the Nijmegen Telephonic Exacerbation Assessment System (TEXAS), that can also detect exacerbations that would otherwise be missed when depending solely on exacerbation data from medical records (*Chapter 4*). TEXAS was successfully used to detect exacerbations in the randomised controlled trial described in *Chapter 6*.

In contrast to the numerous studies on trends in COPD prevalence, and despite the huge impact of exacerbations on quality of life, disease progression, and COPD-related costs, so far trends in COPD exacerbation occurrence rates have been neglected in COPD research (*Chapter 3*). There is still no consensus about the exact definition of COPD exacerbation and symptoms- and event-based definitions are frequently used.²³ This could hamper uniform coding of exacerbations and comparisons between studies. To give more insight into exacerbation trends, there is a need for long-term recording of COPD exacerbations by valid registration databases that record detailed information on both symptom worsening and healthcare contacts.

Differences between patients with COPD

According to *Chapter 2*, COPD is becoming more prevalent in women. This finding, which is consistent throughout the literature,⁴⁻⁶ is important to healthcare professionals and researchers as it indicates that female patients deserve more attention. For example, the majority of participants included in COPD trials are still male; this may impede the application of trial results to both sexes. However, prevalence rates do not reflect the impact of COPD on the level of the patient. Female patients report more COPD-associated anxiety and depression, poorer quality of life, worse dyspnoea, and more exacerbations than male patients.^{24,25} This suggests that the perceived impact of COPD may differ between patients or that patients may present the impact differently. COPD disease management strategies should take differences between patients into account and COPD self-management strategies are therefore indispensable. They are tailor-made, thereby helping healthcare professionals to understand the impact of COPD on the individual patient.

Self-management strategies to alleviate the impact of COPD

The study described in *Chapter 6* was unable to show positive effects on the primary outcome quality of life in COPD patients in general practice, even though the intervention was based on the successful self-management programme *Living Well with COPD*. This programme has previously been shown to reduce hospital

admissions and improve health status in secondary care.²⁶ Other randomised trials conducted in primary care also failed to demonstrate positive effects on ultimate outcomes, such as quality of life, exacerbation frequency, or hospitalisation.²⁷⁻²⁹ In contrast, the evidence base of COPD self-management programmes in secondary care is growing.³⁰⁻³³ These findings suggest that self-management interventions are more effective in secondary than in primary care and that we should be reluctant with recommending self-management in general practice. However, we have to be careful when drawing conclusions from only a limited number of primary care studies. If we want to reach further, we have to realise that research on and implementation of self-management strategies is complex and that success depends on various factors. From the recent studies on COPD self-management, including those reported in the *Chapters 5, 6, and 7*, important lessons have been learned about the process of self-management, the components of the programme, the healthcare system, the provider, and the patient context that warrant proceeding in primary care practice and research.

Process of self-management

The most important aim of self-management interventions is to modify inappropriate behaviour and to reinforce and maintain new healthy behaviour (*Chapter 5*). According to figure 1 presented in *Chapter 5*, behaviour modification will ultimately affect outcomes such as quality of life or hospitalisations. Compared to secondary care, the primary care COPD population represents a much more heterogeneous group of patients with a wide range of disease severity, i.e. varying lung function, health status and functional capacity.³⁴ Overall, COPD patients in primary care tend to have a mild to moderate disease severity according to lung function and a relatively high quality of life (*Chapter 6*). As a consequence, we cannot expect the same effects of self-management programmes on ultimate outcomes in primary care patients as in secondary care patients. But above all, the problems and the needs of the individual patient should determine whether or not a patient receives self-management support, not the setting (primary or secondary care). With behaviour modification as the primary target of the intervention, outcome measures such as self-efficacy, physical activity, smoking cessation, medication adherence, or exacerbation management may be more appropriate primary outcomes or should at least be included as secondary outcomes. As these outcomes reflect the process of self-management, they may help researchers to understand why a self-management programme is successful or fails in supporting the individual patient.

Support for exacerbation management

Exacerbation action plans are the only component of self-management interventions that focus on adequate self-management of acute exacerbations. Action plans are not fixed standardised protocols on how to manage an exacerbation, but are tailored to the individual patient by taking into account his or her prior experiences, knowledge, self-confidence, and skills concerning exacerbations (*Chapter 5*). Action plans aid the recognition and early treatment of exacerbations.³⁵ *Chapter 6* showed that after the first year of the study, patients with an action plan were more likely to increase their bronchodilator use, initiate a course of oral prednisolone and/or antibiotics, and contact the healthcare professional in the course of an exacerbation than patients in the usual care group. It shows that COPD patients in general practice are able to adopt new behaviour styles and it confirms that “as with any other skill, patients experience a learning curve, and need to practice using their action plan” (*Chapter 5*). However, both time and the occurrence of exacerbations are needed for a learning curve. This may explain why short-term studies (up to 1 year only) may fail to find positive effects on self-management behaviour. *Chapter 7* demonstrated that a written action plan decreases symptom recovery time with clinical and statistical significance. This finding was confirmed in a trial on the effects of an isolated individualised exacerbation action plan.³⁶ Obviously, adherence to exacerbation action plans affect the exacerbation itself. Whether it also has impact on complications such as hospital admission and mortality has not yet been confirmed.³⁷ More studies using isolated exacerbation action plans are needed, as exacerbation complications may also be influenced by other parts of the self-management programme, such as stimulating physical activity³⁸ and adherence to inhalation therapy.³⁹ The effects on the recognition, treatment, and recovery of exacerbations justify the use of individualised action plan in daily COPD care, particularly in general practice where unreported exacerbations seems to be a serious problem (as stated earlier).

Not all patients adhere to an exacerbation action plan. In less than 50% of exacerbations, patients followed the instruction to increase their bronchodilator use (*Chapter 6*), and in only 40% patients initiated their standing prescriptions of prednisolone and antibiotics within three days of exacerbation onset (*Chapter 7*). Predictors of adherence are younger age, receiving influenza vaccination, having cardiac co-morbidity, and having more severe airflow obstruction (*Chapter 7*). Also, living with others has previously emerged as a predictor of successful exacerbation management.³⁷ Physicians should be aware that there is a group of patients that fail to adhere to the action plan instructions. The above mentioned predictors are helpful to pay specific attention to these patients, but more research is needed on the reasons why patients may fail to adhere to action plans, and if and how this can be modified.

Organisation of self-management interventions

Self-management programmes are more successful when embedded in a structured COPD disease management programme than when provided in isolation.⁴⁰ The importance of this has also been emphasised in *Chapter 5*. Other components of structured COPD disease management are generally based on the chronic care model for primary care⁴¹ and relate to (i) a well-designed delivery system in which a team of healthcare professionals such as the GP, practice nurse, physiotherapist, and dietician collaborate, (ii) integrated decision support by the use of COPD guidelines and support from a respiratory physician, and (iii) a well-developed clinical information system that aids the delivery system in providing care and monitoring COPD related outcomes. The COPD self-management study described in *Chapter 6* may have failed to demonstrate positive effects due to the absence of other components of the chronic care model. The COPD care in Dutch general practice was less organised at the time of the study (2005) than it is currently. Recently, Dutch general practice collaborations have started with the development of organised and integrated management programmes for patients with COPD in the participating practices. Because they facilitate enhancement of team collaboration, support from secondary care, and monitoring of the care process with well-equipped clinical information systems, these programmes create the desired environment for embedding comprehensive self-management interventions. For example, the *Living Well with COPD* programme that was studied in *Chapter 6* has now been successfully embedded in the COPD management programme of the general practice collaboration in the Arnhem region (www.beter-levenmetcopd.nl). The Kroonluchter integrated disease management programme (Rotterdam area), comprising self-management education, an exercise programme, smoking cessation, exacerbation management, optimal pharmacological therapy, dietary intervention and embedded in a multi-disciplinary integrated primary care team, is another example of a successful COPD management model.⁴²

Providing self-management support

Supporting patients to adequately self-manage their COPD requires not only sufficient disease knowledge and expertise, but also two important skills: 1. the ability to listen and to explore cognitions, the current self-management behaviour and needs of the patient; and 2. to reinforce (if necessary) new behaviour styles. This requires not only time, but also intervention techniques that have been shown to achieve structural behaviour change such as motivational interviewing,⁴³ and often an attitude change in professionals from traditional patient education to shared decision making.⁴⁴ This shift from traditional to collaborative chronic care is illustrated by table 1 in the first chapter of this thesis. However, we cannot expect that professionals already have the skills to correctly apply self-management

strategies. Unfamiliarity, low self-efficacy, and time constraints are important barriers in implementing new COPD disease management interventions in primary care.⁴⁵ Self-management programmes should therefore include well-designed training programmes with ongoing support for healthcare professionals. In the self-management trial described in *Chapter 6*, all participating nurses were trained in how to provide the programme and were observed at least once by a member of the study group who was experienced with providing self-management. Although other recent publications on COPD self-management also clearly describe the training procedures,^{37,46} surprisingly little attention has been paid to the accuracy with which professionals subsequently apply the intervention. As failure to apply the programme correctly will definitely impede the success of self-management, further research is required to break open this black box in the process of self-management.

The context of the patient

Self-management programmes are supposed to be patient-centered, but in their effort to improve a patient's well-being they focus on only one chronic disease. The effects of a programme may be increased when other chronic conditions are also taken into account. This is more realistic, as - according to general practice registration data - more than 60% of patients aged ≥ 65 years suffer from 2 or more chronic diseases.⁴⁷ As a result, the everyday life of patients with COPD may be affected by a complex interaction of several (chronic) conditions. Heart failure, which is apparent in approximately 30% of COPD patients⁴⁸ causes dyspnoea similar to COPD. Depression - which is more common in patients with COPD than in patients with diabetes or without chronic diseases⁴⁹ - seems to moderate the effects of self-management interventions⁵⁰ and is associated with medication non-adherence.⁵¹ Treatment of COPD exacerbations with oral prednisolone may cause hyperglycemia in patients with diabetes and increases the risk of osteoporosis. In addition, we have to realise that modifying behaviour styles, such as quitting smoking, improving exercise and improving medication adherence, is also relevant to other chronic conditions, such as cardiovascular diseases and diabetes. From this point of view, it seems ethically and economically incorrect to entangle a patient with multimorbidity in three different chronic disease management programmes (e.g. COPD, diabetes, and cardiovascular disease) that share common components, which is happening at the moment in Dutch primary care. A generic self-management strategy seems to be more appropriate,^{52,53} but further research is needed to establish its benefits on self-efficacy, self-management behaviour, and health status.

Next to the medical context, the social context of the patient should be taken into account when applying self-management strategies. Social support shows a strong association with improved quality of life in patients with COPD⁵⁴ and with patient's self-management behaviour.^{37,55,56} In the *Living Well with COPD* programme,

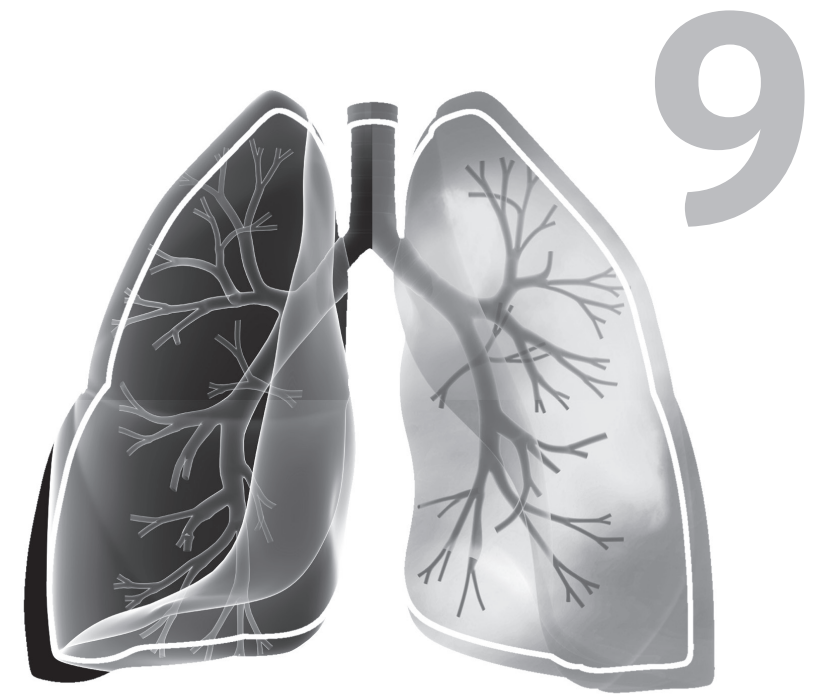
as described in *Chapter 6*, the attendance of a spouse or companion during the sessions was encouraged. However, whether this influenced the outcomes of the study was not evaluated. More research is needed on how social support can be used to improve self-management support in patients.

To become familiar with both the medical and social context of a patient with COPD (or any other chronic disease) requires continuity of care and an extended personal relationship between healthcare professional and patient. This is why general practice medicine or family medicine - where the total medical care of a patient is coordinated during the course of his or her life - is an excellent platform for self-management support. However, we have to reach beyond the echelons of primary care, as effective individualised self-management support can only be achieved in close collaboration with secondary care, where extensive disease knowledge and management expertise is available.

References

1. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease. Revised 2011. Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD): Available from URL: <http://www.goldcopd.org>. Last updated December 2011; Last accessed May 2012.
2. Bellamy D, Bouchard J, Henrichsen S, Johansson G, Langhammer A, Reid J et al. International Primary Care Respiratory Group (IPCRG) guidelines: management of chronic obstructive pulmonary disease (COPD). *Prim Care Respir J*. 2006;15:48-57.
3. Soriano JB, Ancochea J, Miravittles M, Garcia-Rio F, Duran-Tauleria E, Munoz L et al. Recent trends in COPD prevalence in Spain: a repeated cross-sectional survey 1997-2007. *Eur Respir J*. 2010;36:758-65.
4. Vasankari TM, Impivaara O, Heliövaara M, Heistaro S, Liipo K, Puukka P et al. No increase in the prevalence of COPD in two decades. *Eur Respir J*. 2010;36:766-73.
5. Gershon AS, Wang C, Wilton AS, Raut R, To T. Trends in chronic obstructive pulmonary disease prevalence, incidence, and mortality in Ontario, Canada, 1996 to 2007: a population-based study. *Arch Intern Med*. 2010;170:560-565.
6. Akinbami LJ, Liu X. Chronic obstructive pulmonary disease among adults aged 18 and over in the United States, 1998-2009. *NCHS Data Brief*. 2011;1-8.
7. Bourbeau J, Sebaldt RJ, Day A, Bouchard J, Kaplan A, Hernandez P et al. Practice patterns in the management of chronic obstructive pulmonary disease in primary practice: The CAGE study. *Can Respir J*. 2008;15:13-19.
8. Walters JA, Walters EH, Nelson M, Robinson A, Scott J, Turner P et al. Factors associated with misdiagnosis of COPD in primary care. *Prim Care Respir J*. 2011;20:396-402.
9. Zwar NA, Marks GB, Hermiz O, Middleton S, Comino EJ, Hasan I et al. Predictors of accuracy of diagnosis of chronic obstructive pulmonary disease in general practice. *Med J Aust*. 2011;195:168-71.
10. Bottema BJ, Fabels EJ, Van Grunsven PM, van Hensbergen W, Muris JW, van Schayck CP et al. NHG-Standaard CARA bij volwassenen: diagnostiek. *Huisarts Wet*. 1992;35:430-436.
11. van Schayck CP. [The end of the term CARA in sight?] Het einde van de term CARA in zicht? *Ned Tijdschr Geneesk*. 1994;138:1405-8.
12. Geijer RM, Thiadens HA, Smeele IJ, Van der Zwan AA, Sachs AP, Bottema BJ et al. NHG-Standaard COPD en astma bij volwassenen: diagnostiek. *Huisarts Wet*. 1997;40:416-29.
13. Hardie JA, Buist AS, Vollmer WM, Ellingsen I, Bakke PS, Morkve O. Risk of over-diagnosis of COPD in asymptomatic elderly never-smokers. *Eur Respir J*. 2002;20:1117-22.
14. Cerveri I, Corsico AG, Accordini S, Niniano R, Ansaldo E, Anto JM et al. Underestimation of airflow obstruction among young adults using FEV1/FVC < 70% as a fixed cut-off: a longitudinal evaluation of clinical and functional outcomes. *Thorax*. 2008;63:1040-1045.
15. Buist AS, McBurnie MA, Vollmer WM, Gillespie S, Burney P, Mannino DM et al. International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. *Lancet*. 2007;370:741-50.
16. Vanfleteren LE, Franssen FM, Wesseling G, Wouters EF. The prevalence of chronic obstructive pulmonary disease in Maastricht, the Netherlands. *Respir Med*. 2012;106:871-74.
17. Van den Boom G, van Schayck CP, Van Molken MP, Tirimanna PR, den Otter JJ, van Grunsven PM et al. Active detection of chronic obstructive pulmonary disease and asthma in the general population. Results and economic consequences of the DIMCA program. *Am J Respir Crit Care Med*. 1998;158:1730-1738.
18. Albers M, Schermer T, Molema J, Kloek C, Akkermans R, Heijdra Y et al. Do family physicians' records fit guideline diagnosed COPD? *Fam Pract*. 2009;26:81-87.
19. Miravittles M, Soriano JB, Garcia-Rio F, Munoz L, Duran-Tauleria E, Sanchez G et al. Prevalence of COPD in Spain: impact of undiagnosed COPD on quality of life and daily life activities. *Thorax*. 2009;64:863-68.
20. Hill K, Goldstein RS, Guyatt GH, Blouin M, Tan WC, Davis LL et al. Prevalence and underdiagnosis of chronic obstructive pulmonary disease among patients at risk in primary care. *CMAJ*. 2010;182:673-78.

21. Langsetmo L, Platt RW, Ernst P, Bourbeau J. Under-reporting Exacerbation of COPD in Longitudinal Cohort. *Am J Respir Crit Care Med*. 2008;177:396-401.
22. Wilkinson TM, Donaldson GC, Hurst JR, Seemungal TA, Wedzicha JA. Early therapy improves outcomes of exacerbations of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2004;169:1298-303.
23. Effing TW, Kerstjens HA, Monninkhof EM, Van der Valk PD, Wouters EF, Postma DS et al. Definitions of Exacerbations. Does It Really Matter in Clinical Trials on COPD? *Chest*. 2009;136:918-923.
24. Naberan K, Azpeitia A, Cantoni J, Miravittles M. Impairment of quality of life in women with chronic obstructive pulmonary disease. *Respir Med*. 2012;106:367-73.
25. Celli B, Vestbo J, Jenkins CR, Jones PW, Ferguson GT, Calverley PM et al. Sex differences in mortality and clinical expressions of patients with chronic obstructive pulmonary disease. The TORCH experience. *Am J Respir Crit Care Med*. 2011;183:317-22.
26. Bourbeau J, Julien M, Maltais F, Rouleau M, Beupre A, Begin R et al. Reduction of Hospital Utilization in Patients With Chronic Obstructive Pulmonary Disease: A Disease-Specific Self-management Intervention. *Arch Intern Med*. 2003;163:585-91.
27. McGeoch GR, Willsman KJ, Dowson CA, Town GI, Frampton CM, McCartin FJ et al. Self-management plans in the primary care of patients with chronic obstructive pulmonary disease. *Respirology*. 2006;11:611-18.
28. Coultas D, Frederick J, Barnett B, Singh G, Wludyka P. A randomized trial of two types of nurse-assisted home care for patients with COPD. *Chest*. 2005;128:2017-24.
29. Hesselink AE, Penninx BW, van der Windt DA, van Duin BJ, de Vries P, Twisk JW et al. Effectiveness of an education programme by a general practice assistant for asthma and COPD patients: results from a randomised controlled trial. *Patient Educ Couns*. 2004;55:121-28.
30. Effing T, Monninkhof EM, van der Valk PD, van der Palen J, van Herwaarden CL, Partridge MR et al. Self-management education for patients with chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2007;4:CD002990.
31. Sridhar M, Taylor R, Dawson S, Roberts NJ, Partridge MR. A nurse led intermediate care package in patients who have been hospitalised with an acute exacerbation of chronic obstructive pulmonary disease. *Thorax*. 2008;63:194-200.
32. Rice K, Dewan N, Bloomfield H, Grill J, Schult T, Nelson D et al. Disease Management Program for Chronic Obstructive Pulmonary Disease. A Randomized Controlled Trial. *Am J Respir Crit Care Med*. 2010;182:890-896.
33. Koff PB, Jones RH, Cashman JM, Voelkel NF, Vandivier RW. Proactive integrated care improves quality of life in patients with COPD. *Eur Respir J*. 2009;33:1031-38.
34. Siebeling L, Puhan MA, Muggensturm P, Zoller M, ter Riet G. Characteristics of Dutch and Swiss primary care COPD patients - baseline data of the ICE COLD ERIC study. *Clin Epidemiol*. 2011;3:273-83.
35. Walters J, Turnock A, Walters E, Wood-Baker R. Action plans with limited patient education only for exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2010;May 12;(5):CD005074.
36. Trappenburg J, Monninkhof E, Bourbeau J, Troosters T, Schrijvers A, Verheij T et al. Effect of an action plan with ongoing support by a case manager on exacerbation-related outcome in patients with COPD: a multicentre randomised controlled trial. *Thorax*. 2011;66:977-84.
37. Bucknall C, Miller G, Lloyd S, Cleland J, McCluskey S, Cotton M et al. Glasgow supported self-management trial (GSuST) for patients with moderate to severe COPD: randomised controlled trial. *BMJ*. 2012;344:e1060.
38. Benzo RP, Chang CC, Farrell MH, Kaplan R, Ries A, Martinez FJ et al. Physical activity, health status and risk of hospitalization in patients with severe chronic obstructive pulmonary disease. *Respiration*. 2010;80:10-18.
39. Vestbo J, Anderson JA, Calverley PM, Celli B, Ferguson GT, Jenkins C et al. Adherence to inhaled therapy, mortality and hospital admission in COPD. *Thorax*. 2009;64:939-43.
40. Adams SG, Smith PK, Allan PF, Anzueto A, Pugh JA, Cornell JE. Systematic review of the chronic care model in chronic obstructive pulmonary disease. *Arch Intern Med*. 2007;167:551-61.
41. Bodenheimer T, Wagner EH, Grumbach K. Improving primary care for patients with chronic illness. *JAMA*. 2002;288:1775-79.
42. Kruis AL, van Adrichem J, Erkelens MR, Scheepers H, In 't Veen H, Muris JW et al. Sustained effects of integrated COPD management on health status and exercise capacity in primary care patients. *Int J Chron Obstruct Pulmon Dis*. 2010;5:407-13.
43. Effing T, Bourbeau J, Vercoulen J, Apter AJ, Coultas D, Meek P et al. Self-management programmes for COPD: moving forward. *Chron Respir Dis*. 2012;9:27-35.
44. Bodenheimer T, Lorig K, Holman H, Grumbach K. Patient self-management of chronic disease in primary care. *JAMA*. 2002;288:2469-75.
45. Perez X, Wisnivesky JP, Lurslurchachai L, Kleinman LC, Kronish IM. Barriers to adherence to COPD guidelines among primary care providers. *Respir Med*. 2012;106:374-81.
46. Fan VS, Gaziano JM, Lew R, Bourbeau J, Adams SG, Leatherman S et al. A Comprehensive Care Management Program to Prevent Chronic Obstructive Pulmonary Disease Hospitalizations: A Randomized, Controlled Trial. *Ann Intern Med*. 2012;156:673-83.
47. Uijen AA, van de Lisdonk EH. Multimorbidity in primary care: prevalence and trend over the last 20 years. *Eur J Gen Pract*. 2008;14 Suppl 1:28-32.
48. Rutten FH, Cramer MJ, Grobbee DE, Sachs AP, Kirkels JH, Lammers JW et al. Unrecognized heart failure in elderly patients with stable chronic obstructive pulmonary disease. *Eur Heart J*. 2005;26:1887-94.
49. van den Bemt L, Schermer T, Bor H, Smink R, van Weel-Baumgarten E, Lucassen P et al. The risk for depression comorbidity in patients with COPD. *Chest*. 2009;135:108-14.
50. Jerant A, Kravitz R, Moore-Hill M, Franks P. Depressive symptoms moderated the effect of chronic illness self-management training on self-efficacy. *Med Care*. 2008;46:523-31.
51. Khmour MR, Hawwa AF, Kidney JC, Smyth BM, McElroy JC. Potential risk factors for medication non-adherence in patients with chronic obstructive pulmonary disease (COPD). *Eur J Clin Pharmacol*. 2012;Apr 5. [Epub ahead of print].
52. Elzen H, Slaets JP, Snijders TA, Steverink N. Evaluation of the chronic disease self-management program (CDSMP) among chronically ill older people in the Netherlands. *Soc Sci Med*. 2007;64:1832-41.
53. Kennedy A, Reeves D, Bower P, Lee V, Middleton E, Richardson G et al. The effectiveness and cost effectiveness of a national lay-led self care support programme for patients with long-term conditions: a pragmatic randomised controlled trial. *J Epidemiol Community Health*. 2007;61:254-261.
54. Arne M, Lundin F, Boman G, Janson C, Janson S, Emtner M. Factors associated with good self-rated health and quality of life in subjects with self-reported COPD. *Int J Chron Obstruct Pulmon Dis*. 2011;6:511-519.
55. Wang KY, Sung PY, Yang ST, Chiang CH, Perng WC. Influence of family caregiver caring behavior on COPD patients' self-care behavior in Taiwan. *Respir Care*. 2012;57:263-72.
56. Kara Kasikçi M, Alberto J. Family support, perceived self-efficacy and self-care behaviour of Turkish patients with chronic obstructive pulmonary disease. *J Clin Nurs*. 2007;16:1468-78.



Summary

Samenvatting

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Bibliography

Summary

This thesis describes the importance and effects of self-management strategies for COPD and its exacerbations. Also, trends in the impact of COPD on primary care are examined, as well as the importance of adequate exacerbation measurement. This information helps to understand the role of self-management for COPD and its exacerbations in daily practice and clinical studies.

Chapter 1 introduces the background and main objectives of this thesis. The current prevalence of Chronic Obstructive Pulmonary Disease (COPD) casts a heavy burden on healthcare systems worldwide. People with COPD may suffer from mild to very severe symptoms, such as dyspnoea, cough, sputum, and fatigue, that can have an immense impact on daily functioning and quality of life. Besides, COPD is characterised by exacerbations, i.e. periods of sustained symptom worsening that may be very disabling and require medical attention. The impact of COPD and its exacerbations on a patient's life is progressive, but may vary between and within patients. Despite the current impact of COPD on patients and healthcare systems, there is still a high degree of undertreatment among patients with COPD, particularly in primary care. If the burden of COPD is to be relieved, new strategies to manage the disease are essential. Consequently, there is a need for COPD management that is dynamic and continuously tailored to the individual patient's needs by considering the impact of all different aspects of the disease at any moment in the disease progress. In this context, COPD self-management interventions are promising. Briefly, self-management strategies comprise comprehensive chronic care tailored to individual needs and focused on the enhancement of patients' abilities to self-manage their disease proactively.

This thesis addresses the following objectives:

- To describe long-term trends in COPD prevalence and exacerbation occurrence rates in Dutch general practice.
- To assess the validity of an automated telephonic exacerbation assessment system to record exacerbation rates in prospective clinical studies and to relate its results to other exacerbation detection tools.
- To describe the concept and practice of self-management and its potential role in the prevention and early treatment of COPD exacerbations.
- To assess the long-term effects on quality of life of two different modes of COPD disease management in general practice, i.e. comprehensive self-management and routine monitoring.
- To assess the effects of a written action plan for COPD exacerbations on exacerbation recovery time and unscheduled healthcare utilisation.

Chapter 2 describes the impact of COPD and its exacerbations on a Dutch general practice population. We performed a trend analysis on data regarding COPD diagnosis and exacerbation occurrence that we retrieved from the Continuous Morbidity Registration Nijmegen database for the period 1980–2006. The Continuous Morbidity Registration Nijmegen is a valid prospective cohort study in which four Dutch general practices with a registered practice population of approximately 15 000 subjects in the Nijmegen area have participated since 1967. We found that between 1980 and 2006, the overall prevalence of COPD decreased from 72.7 to 54.5 per 1000 patients per year. The exacerbation rate decreased from 44.1 to 31.5 per 100 patients per year and the percentage of patients with COPD who had exacerbations declined from 27.6% to 21.0% per year, independent of sex, age, and socioeconomic status. COPD prevalence increased significantly in women, in particular those aged ≥ 65 years with low socioeconomic status. Our results suggest a reduction of the COPD burden on Dutch primary care. Besides, the increasing prevalence in women indicates a need to focus on this particular subgroup in COPD management and research.

Chapter 3 presents our comments on the results of a Canadian trend study on COPD prevalence. The Canadian investigators found a substantial increase in COPD prevalence in the last decade using a population-based, health administrative database. Although these results seem to contradict our findings of Chapter 2, the increase was mainly caused by an increasing prevalence in women while the rise of prevalence in men flattened. This is in line with our finding that women are catching up with men rapidly. Also, the Canadian study showed a decreasing incidence of COPD, which – in our opinion – could have been provoked (partly) by an increased physician awareness of COPD over time leading to fewer false-positive diagnoses. Although the Canadian authors recognised the importance of exacerbations as an outcome, exacerbations were not analysed in their study.

Chapter 4 describes a study in which we assessed the validity of an automated telephonic exacerbation assessment system (TEXAS) and compared its outcomes with existing tools. Commonly used methods are based on periodic (retrospective) questionnaires, patient diary cards and medical record review. These methods of data collection often lack validity testing and have in common that they are rather time consuming for patients and/or researchers, often at the expense of patients' compliance. TEXAS consists of questions regarding changes in respiratory symptoms, use of healthcare resources and use of respiratory medication in the 2 weeks prior to the call. The questions are based on common and recommended definitions of exacerbation, i.e. symptom- and event-based exacerbations. Once every 2 weeks, a patient with COPD receives an automated telephone call with a

real life voice on the day and time of his/her own preference. Independent of the exacerbation definition used, the validity of TEXAS was high. Detection rates and compliance differed extensively between the different tools, but were highest with TEXAS. We conclude that TEXAS is a valid tool to assess COPD exacerbation rates in prospective clinical studies and that using different tools to record exacerbations strongly affects exacerbation occurrence rates.

Chapter 5 describes the concept and practice of COPD self-management with a specific focus on prevention and early treatment of COPD exacerbations. Self-management can be described as a set of skilled behaviors and refers to the various tasks that individuals carry out for the management of their condition. A self-management programme in COPD targets the integration of effective interventions that are recognized to be effective in disease control, such as healthy life habits (smoking cessation, regular exercise) and self-management skills (adherence to medication, breathing techniques and positioning, early recognition and prompt treatment of exacerbations). Self-management support is not only about education. It aims at behavior modification and maintenance by improving the desired skills, knowledge, and self-efficacy. This will eventually lead to improved outcomes. However, it takes time to modify behaviour; this should be realized by researchers and healthcare providers. Successful self-management programmes are based on organization and practice that include accurate self-management strategies, enhance patients' self-efficacy and specific skills, and are supported by a practice team and a case manager to optimize disease control and follow-up. Self-management of COPD exacerbations aims at early recognition and treatment of exacerbations in order to prevent complications such as deterioration in quality of life and hospitalisations. Self-management of exacerbations should be an important part of COPD care as under-reporting of COPD exacerbations is a widespread phenomenon. Individualised action plans, whether embedded or not in a comprehensive self-management intervention, are useful in providing the patient a guideline for proper management of an exacerbation.

Chapter 6 presents the results of a randomised controlled trial in which we assessed the long-term effects of comprehensive self-management and routine monitoring on quality of life, frequency and patients' management of exacerbations, and self-efficacy in COPD patients in general practice. Patients with COPD were randomly allocated to (i) a modified version of the self-management programme *Living Well with COPD* as an adjunct to usual care consisting of 4 tailored sessions with ongoing telephonic support by a practice nurse, (ii) routine monitoring consultations based on national COPD guidelines as an adjunct to usual care consisting of 2 to 4 structured consultations per year with a practice nurse, or (iii)

usual care alone, i.e., contacts with the general practitioner at patients' own initiative. At 24 months we found no statistical significant differences between the three groups in COPD specific quality of life or COPD self-efficacy. Patients in the self-management group seemed more capable of appropriately managing exacerbations than in the usual care group in terms of increasing the use of bronchodilators (46.5% vs 26.5% exacerbations, respectively) and initiating prednisolone and/or antibiotics (15.5% vs 4.9% exacerbations, respectively). This study was well powered, had a long follow-up and included self-efficacy and behaviour change as secondary outcomes. However, it could not confirm the effects of *Living Well with COPD* on disease-specific quality of life as previously observed in a Canadian trial. A high mean baseline quality of life score limited the room for improvement in our primary outcome. In addition, we observed individual differences among the practice nurses in COPD education, experiences, and attitude that may have influenced the application of the self-management programme to the patients. The Dutch chronic care structure has evolved since the time of our study which benefits the chance of self-management success; there is a better prepared delivery system with collaboration between healthcare providers, more and better equipped practice nurses, and a continuum of care to enhance self-management behaviour, organized decision support from secondary care, and integration of clinical information systems to support both the professional and the patient.

Chapter 7 describes a study on the effect of adherence to a written action plan on exacerbation recovery time and unscheduled healthcare utilization. As a secondary objective, factors associated with action plan adherence were explored. In 1-year prospective cohort study embedded in a randomised controlled trial we collected exacerbation data of 252 patients with COPD who received a written action plan for prompt treatment of exacerbations. The action plan included instructions to initiate standing prescriptions for both antibiotics and prednisone within 3 days of exacerbation onset. Following the instructions was defined as adherence to the action plan. Of the 288 exacerbations reported by 143 patients, 217 exacerbations reported by 119 patients (53.8% male, mean age 65.4 years, postbronchodilator forced expiratory volume in 1 s (FEV1) 43.9% predicted) could be used in the analyses. In 40.1% of exacerbations, patients adhered to their written action plan. Adherence reduced exacerbation recovery time with statistical ($p < 0.0001$) and clinical (-5.8 days) significance, but did not affect unscheduled healthcare utilisation (OR 0.94, 95% CI 0.49 to 1.83). Factors associated with an increased likelihood of adherence were influenza vaccination, cardiac comorbidity, younger age and lower FEV1 as percentage predicted. The findings of this study suggest that action plans deserve a more prominent role in exacerbation management. However, less than half of the exacerbations were treated according to the instructions. Sufficient time

and supportive coaching for patients should be allowed to improve the management of exacerbations. Knowing the factors that are associated with proper and prompt utilisation of an action plan permits healthcare professionals to better focus their self-management support on appropriate patients. However, additional research on this topic is needed.

Chapter 8 provides an overall view on the chapters of this thesis. The impact of COPD and COPD exacerbations on primary care and the role of COPD self-management as innovative disease management strategy to diminish the impact are discussed in the light of the results described in this thesis and with respect to current literature and future perspectives. The results of the trend study suggest a reduction of the COPD burden on Dutch primary care, but missed diagnosis and misdiagnosis of COPD and under-reporting of exacerbations should be taken into account. Besides, prevalence rates do not reflect (differences in) the impact of COPD on the level of the patient. Self-management strategies may alleviate the impact of COPD, but we have to realise that research on and implementation of self-management strategies is complex and that success depends on various factors. From the studies described in this thesis, important lessons have been learned about the process of self-management, the components of the programme, the healthcare system, the provider, and the patient context that warrant proceeding in primary care practice and research.

Samenvatting

Dit proefschrift behandelt het belang en de effecten van zelfmanagementinterventies voor COPD en COPD exacerbaties. Daarnaast beschrijft dit proefschrift hoe de impact van COPD op de huisartsgeneeskunde in de laatste decennia is veranderd en het belang van het adequaat meten van COPD exacerbaties in wetenschappelijke studies. Deze informatie helpt ons bij het bepalen van de rol van zelfmanagement voor COPD en exacerbaties in de dagelijkse praktijk en in klinisch wetenschappelijk onderzoek.

Hoofdstuk 1 beschrijft de achtergronden en de doelen van dit proefschrift. COPD is een afkorting van Chronic Obstructive Pulmonary Disease, een verzamelnaam van chronisch obstructieve en langzaam progressieve longaandoeningen waaronder chronische bronchitis en longemfyseem. COPD is een veel voorkomende chronische aandoening en de economische en maatschappelijke gevolgen drukken zwaar op gezondheidssystemen wereldwijd. Mensen met COPD ervaren matige tot zeer ernstige klachten, zoals benauwdheid, hoesten, last van slijm en vermoeidheid. Deze klachten leiden tot beperkingen in het dagelijks functioneren en hebben een negatieve invloed op de kwaliteit van leven. COPD wordt gekenmerkt door het optreden van exacerbaties, periodes van aanhoudende klachtenverergeringen met ernstige beperkingen. De invloed van COPD en de bijbehorende exacerbaties op het leven van de patiënt is progressief, maar varieert tussen patiënten en met de tijd. Ondanks de huidige impact van COPD op patiënten en zorgsystemen bestaat er nog steeds een enorme onderbehandeling, vooral in de huisartspraktijk. Als we de druk van COPD willen verlichten, zijn nieuwe behandelstrategieën nodig. Daarbij is vooral behoefte aan behandelmethoden die dynamisch zijn en voortdurend kunnen worden aangepast aan de behoeftes van de individuele patiënt door rekening te houden met alle aspecten van de ziekte op elk moment in het ziekteproces. In deze context zijn COPD zelfmanagementprogramma's veelbelovend.

Een zelfmanagementprogramma biedt chronische zorg in alle facetten en is afgestemd op de behoeftes van de individuele patiënt. Een zelfmanagementprogramma richt zich op het bevorderen van de mogelijkheden die een patiënt heeft om zelf zijn aandoening proactief te kunnen “managen”.

Dit proefschrift heeft de volgende doelstellingen:

- Het beschrijven van langetermijnveranderingen in de prevalentie van COPD en COPD exacerbaties in de Nederlandse huisartspraktijk.
- Het vaststellen van de validiteit van een geautomatiseerd belsysteem voor het detecteren van exacerbaties in prospectieve klinische studies en het vergelijken van de resultaten met andere exacerbatie detectiesystemen.

- Het beschrijven van het concept en de praktische uitvoering van zelfmanagementondersteuning en de rol van zelfmanagement in het voorkomen en vroegtijdig behandelen van exacerbaties.
- Het vaststellen van de langetermijneffecten op de kwaliteit van leven van twee verschillende behandelmethoden voor COPD, namelijk een COPD-specifiek zelfmanagementprogramma en geprotocolleerde routinematige controles.
- Het vaststellen van de effecten van een actieplan voor COPD exacerbaties op de herstelduur van exacerbaties en zorgconsumptie.

Hoofdstuk 2 beschrijft de impact van COPD en COPD exacerbaties op de Nederlandse huisartspraktijk. Wij bestudeerden de langetermijnveranderingen in de prevalentie van COPD en COPD exacerbaties door gebruik te maken van registratiegegevens uit het databestand van de Continue Morbiditeit Registratie (CMR) Nijmegen over de periode 1980–2006. De Continue Morbiditeit Registratie (CMR) Nijmegen is een valide prospectieve cohortstudie waaraan vier huisartspraktijken uit de regio Nijmegen met een totale praktijkpopulatie van ongeveer 15000 patiënten deelnemen sinds 1967. Wij vonden dat tussen 1980 en 2006 de prevalentie van COPD afnam van 72.7 tot 54.5 patiënten per 1000 patiënten per jaar. De exacerbatiefrequentie nam af van 44.1 tot 31.5 exacerbaties per 100 patiënten per jaar en het percentage COPD patiënten met exacerbaties nam af van 27.6% tot 21.0% per jaar, onafhankelijk van geslacht, leeftijd of sociaaleconomische status. De prevalentie van COPD steeg significant bij vrouwen, vooral met een leeftijd ≥ 65 jaar met een lage sociaaleconomische status. Onze resultaten lijken te wijzen op een afname van de druk van COPD op de Nederlandse huisartspraktijk. Bovendien suggereert de toenemende prevalentie bij vrouwen dat zorg en onderzoek zich meer zou moeten richten op deze subgroep van patiënten.

Hoofdstuk 3 geeft ons commentaar weer op een Canadese studie naar langetermijnveranderingen in de prevalentie van COPD. De Canadese onderzoekers vonden een substantiële stijging in de prevalentie van COPD gedurende het laatste decennium. Zij maakten daarbij gebruik van gegevens uit een groot bestand met bevolkingsgegevens. Hoewel hun resultaten op het eerste gezicht in tegenspraak lijken te zijn met onze bevindingen uit Hoofdstuk 2, blijkt de stijging vooral te komen door een toenemende prevalentie bij vrouwen terwijl de prevalentie bij mannen stabiliseerde. Deze resultaten sluiten aan bij onze bevinding dat vrouwen bezig zijn met een inhaalslag ten opzichte van mannen. Daarnaast vonden de Canadezen een dalende incidentie (dat wil zeggen, het aantal *nieuwe* COPD patiënten per jaar). Naar onze mening zou dat gedeeltelijk veroorzaakt kunnen zijn doordat een toenemende aandacht voor COPD onder dokters kan leiden tot een afname in het aantal verkeerd gediagnosticeerde patiënten. Hoewel de Canadezen erkenden dat

het belangrijk is om exacerbaties als uitkomst in onderzoeken mee te nemen, lieten zij dat na in hun eigen studie.

Hoofdstuk 4 beschrijft een studie waarin we de validiteit vaststelden van een geautomatiseerd belsysteem voor het detecteren van exacerbaties (TEXAS) in klinische studies. Bovendien vergeleken we het aantal gedetecteerde exacerbaties met de uitkomsten van bestaande detectiemethoden. Bestaande methoden zijn vooral gebaseerd op het afnemen van vragenlijsten, het verzamelen van dagboekjes of het analyseren van patiëntendossiers. De validiteit van deze methoden is twijfelachtig. Daarnaast vergen zij veel tijd van onderzoekers en patiënten, wat ten koste gaat van de volledigheid van de verzamelde gegevens. TEXAS bestaat uit vragen met betrekking tot veranderingen in luchtwegklachten, het gebruik van medische zorg en het gebruik van (luchtweg)medicatie in de twee weken voorafgaand aan het telefonisch contact. De vragen zijn gebaseerd op veel voorkomende en algemeen geaccepteerde definities van exacerbatie, namelijk klachtgerelateerde en zorggerelateerde definities. Eén keer per twee weken belt TEXAS op de dag en tijdstip van voorkeur de patiënt die een tiental vragen binnen enkele minuten met “ja” of “nee” beantwoordt. Wij vonden dat, onafhankelijk van de definitie die we gebruikten, de validiteit van TEXAS hoog is. De gedetecteerde exacerbatiefrequenties en de volledigheid van de gegevens verschilden enorm tussen de verschillende methoden, maar waren het hoogste met TEXAS. Wij concludeerden dat TEXAS een betrouwbare methode is om exacerbaties te detecteren in prospectief klinisch onderzoek en dat het gebruik van verschillende detectiemethoden de gevonden exacerbatiefrequentie sterk beïnvloedt.

Hoofdstuk 5 beschrijft het concept en de uitvoering van zelfmanagementondersteuning voor patiënten met COPD. In het bijzonder besteedt dit hoofdstuk aandacht aan het voorkómen van en tijdig reageren op exacerbaties. Zelfmanagement verwijst naar alle handelingen en gedragingen die een persoon toepast bij het omgaan met zijn chronische aandoening. Een COPD zelfmanagementprogramma richt zich op het integreren van gedragingen die effectief zijn gebleken in het verbeteren van de ervaren ziektelast, zoals een gezonde leefstijl (bijvoorbeeld stoppen met roken, voldoende lichaamsbeweging) en vaardigheden (bijvoorbeeld medicatietrouw, ademhalingstechnieken, energie besparen, tijdig herkennen van en adequaat reageren op exacerbaties). Zelfmanagementondersteuning richt zich niet alleen op het verstrekken van informatie of onderwijzen van de patiënt. De ondersteuning heeft als doel het bevorderen en in stand houden van gedragsveranderingen door het verbeteren van de gewenste vaardigheden, kennis en self-efficacy (dat wil zeggen, het vertrouwen dat iemand heeft in zijn eigen handelen). Uiteindelijk zullen zo de gewenste doelen kunnen worden behaald. Gedragsveran-

deringen kosten echter tijd en hiermee dient rekening te worden gehouden in onderzoek en de dagelijkse praktijk. Succesvolle zelfmanagementprogramma's worden aangeboden door een case-manager (coach) ondersteund door een team van zorgverleners en maken deel uit van een gestructureerde organisatie gericht op optimale ziektecontrole en -monitoring. Zelfmanagementondersteuning voor exacerbaties richt zich op het vroegtijdig herkennen en behandelen van exacerbaties om zo complicaties zoals verslechtering in de kwaliteit van leven en ziekenhuisopnames te voorkomen. Ondersteuning gericht op het gedrag ten tijde van exacerbaties vormt een belangrijke component van de COPD zorg, omdat onderreportage van exacerbaties een wijdverspreid fenomeen is. Geïndividualiseerde actieplannen, al dan niet ingebed in een uitgebreid zelfmanagementprogramma, helpen de patiënt om adequaat om te gaan met exacerbaties.

Hoofdstuk 6 beschrijft de resultaten van een gerandomiseerd gecontroleerd experiment waarin we de langetermijneffecten onderzochten van een uitgebreid zelfmanagementprogramma en geprotocolleerde routinematige controles op kwaliteit van leven, frequentie en zelfmanagement van exacerbaties en self-efficacy bij patiënten met COPD in de huisartspraktijk. Patiënten met COPD werden geloot over (i) een aangepaste versie van het Canadese zelfmanagementprogramma *Living Well with COPD* als aanvulling op de gebruikelijke zorg bestaande uit vier op maat gemaakte sessies gevolgd door telefonische ondersteuning aangeboden door de praktijkondersteuner, (ii) geprotocolleerde routinematige controles gebaseerd op nationale COPD richtlijnen als aanvulling op de gebruikelijke zorg bestaande uit twee tot vier gestructureerde consulten per jaar bij de praktijkondersteuner, of (iii) alleen gebruikelijke zorg, dat wil zeggen consulten bij de huisarts op initiatief van de patiënt zelf. Op 24 maanden na de start van de studie vonden wij geen statistisch significante verschillen tussen de drie groepen wat betreft kwaliteit van leven of self-efficacy. Patiënten in de zelfmanagementgroep leken wel beter in staat te zijn om adequaat om te gaan met exacerbaties vergeleken met patiënten die gebruikelijke zorg ontvingen; bij meer exacerbaties verhoogden zij hun luchtwegverwijder (46.5% vs 26.5% exacerbaties) en werd prednisolon en/of antibiotica gestart (15.5% vs 4.9% exacerbaties). Onze studie had voldoende power voor het vinden van effecten, maakte gebruik van een langdurige follow-up en onderzocht ook self-efficacy en gedragsverandering. Toch konden wij niet het positieve effect van *Living Well with COPD* op kwaliteit van leven bevestigen, zoals dat eerder in een Canadees onderzoek was aangetoond. Een hoog gemiddeld niveau in kwaliteit van leven aan het begin van de studie bood weinig ruimte tot verbetering. Bovendien merkten wij grote individuele verschillen tussen praktijkondersteuners in COPD kennis, ervaring en attitude die mogelijk de zelfmanagementondersteuning van patiënten beïnvloed hebben. Sinds de uitvoering van onze studie is het chronische

zorgsysteem in de Nederlandse eerste lijn drastisch veranderd. Dit komt ten goede aan de kansen op succes van zelfmanagementondersteuning; de samenwerking tussen zorgverleners is verbeterd, praktijkondersteuners worden beter voorbereid en begeleid, er is meer continuïteit in de chronische zorg waardoor het proces van zelfmanagement kan blijven worden ondersteund, kennis en kunde uit de tweede lijn is meer geïntegreerd en er wordt op een betere manier gebruik gemaakt van elektronische huisartseninformatiesystemen (HIS) en/of keteninformatiesystemen (KIS) ter ondersteuning van patiënt en zorgverlener.

Hoofdstuk 7 beschrijft een studie naar de effecten van het correct uitvoeren van een exacerbatie actieplan op de herstelduur van exacerbaties en gebruik van zorg. Als tweede doel verkenden wij welke factoren geassocieerd zijn met het correct uitvoeren van de instructies uit het actieplan. In een 1-jaar durend onderzoek volgden wij een groep van 252 patiënten met COPD en verzamelden wij gegevens over exacerbaties. Het onderzoek maakte deel uit van een gerandomiseerd gecontroleerd experiment dat plaatsvond in Canada. Alle patiënten ontvingen een actieplan om exacerbaties tijdig te herkennen en adequaat te behandelen. Het actieplan bevatte de instructie om te starten met op voorhand verstrekte recepten prednisolon en antibioticum wanneer de verergering van luchtwegklachten niet binnen drie dagen verbeterde. Het uitvoeren van deze instructie definieerden wij als het correct uitvoeren van het actieplan. Van de 288 exacerbaties die door 143 patiënten werden gemeld, konden wij 217 exacerbaties van 119 patiënten (53.8% man, gemiddelde leeftijd 65.4 jaren, postbronchodilatatoire forced expiratory volume in 1 s (FEV1) 43.9% van voorspeld) analyseren. In 40.1% van de exacerbaties voerden de patiënten de instructies van het actieplan correct uit. Dit leidde tot een statistisch significante ($p < 0.0001$) en klinisch relevante (-5.8 dagen) vermindering van de duur van een exacerbatie, maar zorgde niet voor een vermindering in het gebruik van zorg (OR 0.94, 95% CI 0.49-1.83). Factoren die geassocieerd zijn met een grotere kans op het correct uitvoeren van het actieplan waren het nemen van de griep prik, het hebben van een hartaandoening, een jongere leeftijd en een slechtere longfunctie. Onze resultaten suggereren dat een actieplan een belangrijke plek behoort in te nemen bij exacerbatie management. Slechts in minder dan de helft van de exacerbaties voerden de patiënten hun actieplan correct uit. Voldoende tijd voor het opdoen van ervaring en goede ondersteuning zijn voorwaarden om exacerbatie management te verbeteren. Kennis van factoren die geassocieerd zijn met het gebruiken van een actieplan helpt zorgverleners de juiste patiënten beter te begeleiden. Meer onderzoek is echter nodig.

Hoofdstuk 8 bediscussieert, aan de hand van de eerdere hoofdstukken en de meest recente wetenschappelijke literatuur, de invloed van COPD en COPD exacer-

baties op de huisartspraktijk en de rol van zelfmanagement als innovatieve zorgstrategie bij het verminderen van deze invloed. De resultaten van de trendstudie uit Hoofdstuk 2 suggereren een vermindering van de druk van COPD op de Nederlandse huisartspraktijk, maar houden geen rekening met door eerdere studies aangetoonde gemiste COPD diagnoses, verkeerde COPD diagnoses en onderrapportage van exacerbaties. Bovendien weerspiegelen prevalentiecijfers niet de (verschillen in) impact van COPD op het niveau van de patiënt. Zelfmanagementprogramma's hebben de potentie om de impact van COPD te verminderen, maar we moeten ons realiseren dat onderzoek naar en implementatie van zelfmanagementondersteuning complex is en dat succes afhangt van verschillende factoren. De studies die beschreven staan in dit proefschrift leren ons over het proces van zelfmanagement, de componenten en uitvoering van een zelfmanagementprogramma, de organisatie van het zorgsysteem, het belang van de zorgverlener en de context van de patiënt. De resultaten van dit proefschrift dagen ons uit om verder te gaan met onderzoek naar en implementatie van zelfmanagement in de (huisarts)praktijk.

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About the author

On 3 January 1978 Erik Bischoff was born in Heerlen, the Netherlands. He grew up in Brunssum and graduated from secondary school (gymnasium) in Hoensbroek (St Janscollege). From 1996 to 2000 he studied Biomedical Health Sciences at the Radboud University Nijmegen and he obtained his Master in the field of Toxicology. His research projects on chemical sensitivity in symptomatic Dutch United Nations Cambodia Veterans and respiratory symptoms in asthmatic school children in Utrecht resulted in several international publications. Between 2000 and 2005 he studied Medicine at the Radboud University Nijmegen. In 2005, he started with the General Practitioner (GP) vocational training at the same university. He combined his training with a PhD programme. During this combined training period he founded – together with colleague PhD trainees - the PhD Council of the Nijmegen Centre of Evidence Based Practice (NCEBP). In 2007, Erik worked as a researcher at the Chest Institute of the McGill University in Montreal, Canada under supervision of Jean Bourbeau, chest physician.

Since 2009, Erik has worked as a GP, currently at the University Health Centre Heyendaal (www.ugc-heyendaal.nl). He is involved in the development of integrated care programmes for COPD and the implementation of self-management in chronic care in the Nijmegen region (Organisatie voor Chronische Eerstelijns Zorg) and Arnhem region (Huisartsenzorg regio Arnhem). His Dutch version of *Living Well with COPD* has been fully implemented in the COPD care programme in the Arnhem region (www.beterlevenmetcopd.nl). Erik coordinates the COPD and asthma care in the Network of Academic General Practices Nijmegen.

Erik received an AGIKO stipend of the Netherlands Organisation for Health Research and Development (ZonMw).

Erik is married with Simone Lardenoije and together with their two daughters Julia and Rosalie they live in Nijmegen.

Over de auteur

Op 3 januari 1978 werd Erik Bischoff geboren in Heerlen. Hij groeide op in Brunssum en behaalde in 1996 zijn gymnasium diploma aan het St Janscollege in Hoensbroek. Van 1996 tot en met 2000 studeerde hij Biomedische Gezondheidswetenschappen aan de Radboud Universiteit Nijmegen met als afstudeerrichting Toxicologie. Zijn afstudeerprojecten naar chemische overgevoeligheid bij Nederlandse VN-soldaten en luchtwegklachten bij astmatische Utrechtse schoolkinderen resulteerden in verscheidene internationale publicaties. Van 2000 tot 2005 studeerde Erik Geneeskunde aan de Radboud Universiteit Nijmegen. Aansluitend startte hij aan dezelfde universiteit met het gecombineerde traject van promotie en huisartsenopleiding (*aiotho*). Hij richtte samen met collega promovendi van het Nijmegen Centre of Evidence Based Practice (NCEBP) de PhD Council op. In de tweede helft van 2007 was Erik als onderzoeker werkzaam aan het Chest Institute van de McGill University in Montreal, Canada onder leiding van longarts Jean Bourbeau.

Sinds 2009 is Erik werkzaam als huisarts in Nijmegen, vanaf 2011 in het Universitair Gezondheidscentrum Heyendaal (www.ugc-heyendaal.nl). Daarnaast is Erik onderzoeker aan de afdeling Eerstelijns geneeskunde van het UMC St Radboud en is hij betrokken bij de vormgeving van de COPD-ketenzorg en zelfmanagement in de regio Nijmegen (Organisatie voor Chronische Eerstelijnszorg) en Arnhem (Huisartsenzorg regio Arnhem). In de regio Arnhem is zijn zelfmanagementprogramma *Living Well with COPD* geïmplementeerd in het COPD-ketenzorgprogramma (www.beter-levenmetcopd.nl). Erik coördineert de COPD- en astmazorg in het Netwerk Academische Huisartspraktijken Nijmegen.

Erik ontving een persoonsgerichte stimulering van ZonMw in de vorm van een Agiko-Stipendium.

Erik is getrouwd met Simone Lardenoije en samen met hun twee dochters Julia en Rosalie wonen zij in Nijmegen.

Bibliography

- Bischoff EW**, Soetekouw PM, de Vries M, Scheepers PT, Bleijenberg G, van der Meer JW. Chemical sensitivity in symptomatic Cambodia veterans. *Arch Environ Health* 2003;58(12):740-45.
- Van Amsterdam JG, **Bischoff EW**, de Klerk A, Verlaan AP, Jongbloets LM, van Loveren H, Opperhuizen A, Zomer G, Hady M, Spijksma FT, Dormans JA, Steerenberg PA. Exhaled NO level and number of eosinophils in nasal lavage as markers of pollen-induced upper and lower airway inflammation in children sensitive to grass pollen. *Int Arch Occup Environ Health* 2003;76(4):309-12.
- Steerenberg PA, **Bischoff EW**, de Klerk A, Verlaan AP, Jongbloets LM, van Loveren H, Opperhuizen A, Zomer G, Heisterkamp SH, Hady M, Spijksma FT, Fischer PH, Dormans JA, van Amsterdam JG. Acute effect of air pollution on respiratory complaints, exhaled NO and biomarkers in nasal lavages of allergic children during the pollen season. *Int Arch Allergy Immunol* 2003;131(2):127-37.
- Van Amsterdam JG, **Bischoff EW**, Hady M, Opperhuizen A, Steerenberg PA. The prevalence of allergic sensitisation in immigrant children in The Netherlands. *Int Arch Allergy Immunol* 2004;133(3):248-54.
- Van Amsterdam JG, Van der Horst-Graat J, **Bischoff E**, Steerenberg P, Opperhuizen A, Schouten E. The effect of vitamin E supplementation on serum DHEA and neopterin levels in elderly subjects. *Int J Vitam Nutr Res* 2005;75(5):327-31.
- Bischoff EW**, Poels PJ, Schermer TR, Van Weel C. Nurse led COPD management: need for individualised outcome. *BMJ* 25 September 2005, *E-letter*. Available at: <http://www.bmj.com/rapid-response/2011/10/31/nurse-led-copd-management-need-individualised-outcome>.
- Bischoff EW**. Koude voeten, natte neuzen [Cold feet, runny noses]. *Huisarts Wet* 2006;49(2):60.
- Bischoff EW**. Te lage bloeddruk brengt het hart in nood [Lowering the blood pressure endangers the heart]. *Huisarts Wet* 2006;49(9):440.
- Bischoff EW**. Focus on COPD disease management. *BMJ* 23 May 2007, *E-letter*. Available at: <http://www.bmj.com/rapid-response/2011/11/01/focus-copd-disease-management>.
- Bischoff EW**. Spirometrie in de eerste lijn [Spirometry in primary care]. *Bijblijven* 2007;23(9):12-20.

- Van den Bemt L, Schermer T, Smeele I, **Bischoff E**, Jacobs A, Grol R, van Weel C. Monitoring of patients with COPD: A review of current guidelines' recommendations. *Respir Med* 2008;102(5):633-41.
- Bourbeau J, **Bischoff EW**, Seden M. Self-management in prevention and early intervention of exacerbations. In: Wedzicha W, Martinez F, eds. *Chronic Obstructive Pulmonary Disease Exacerbations*. New York: Informa Healthcare, 2008:357-368.
- Bischoff E**. Bupropion effectief bij stoppen met roken onder begeleiding van de huisarts [Bupropion benefits counselling for smoking cessation in primary care]. *Ned Tijdschr Geneesk* 2008;152(26):1493.
- Bischoff EW**, Uijen A, van der Wel M. De puber met angst voor een soa [The adolescent with fear of STD]. *Huisarts Wet* 2008;51(13):685-686.
- Bischoff EW**, Uijen A, van der Wel M. Aphthous Ulcers. *BMJ* 2009;339:b2382.
- Bischoff EW**, Schermer TR, Bor H, Brown P, van Weel C, van den Bosch WJ. Trends in COPD prevalence and exacerbation rates in Dutch primary care. *Br J Gen Pract* 2009;59(569):927-33.
- Bischoff E**, Thoonen BP. Zelfmanagement bij patiënten met COPD [Self-management for patients with COPD]. *Modern Medicine* 2009;3A:8-11.
- Hannink J, Lahaije A, **Bischoff E**, van Helvoort H, Dekhuijzen R, Schermer T, Heijdra Y. Dynamic hyperinflation after metronome-paced hyperventilation in COPD - A 2 year follow-up. *Respir Med* 2010;104(11):1700-5.
- Bischoff EW**, Uijen A, van der Wel M. Aphthae. *Praxis (Bern 1994)* 2010;99(11):669-70.
- Bischoff EW**, Crockett AJ, Schermer TR. Trends in population burden of COPD: actual facts or fallacies? *Arch Intern Med* 2010;170:1408-1409.
- Bischoff E**. Toevoeging LWBW aan ICS is niet effectief bij kinderen met astma [Adding LABA to ICS does not benefit children with asthma]. *Huisarts Wet* 2010;53(5):290.
- Bischoff EW**, Hamd DH, Seden M, Benedetti A, Schermer TR, Bernard S, Maltais F, Bourbeau J. Effects of written action plan adherence on COPD exacerbation recovery. *Thorax*. 2011;66:26-31.
- Van Dijk WD, van den Bemt L, van den Haak-Rongen S, **Bischoff E**, van Weel C, In 't Veen JC, Schermer TR. Multidimensional prognostic indices for use in COPD patient care. A systematic review. *Respir Res* 2011;12:151.
- Scherpbier-de Haan N, **Bischoff EW**. Dagelijks azitromycine vermindert COPD-exacerbaties [Daily azitromycin prevents COPD exacerbations]. *Ned Tijdschr Geneesk* 2011;155:A4083.
- Uijen AA, **Bischoff EW**. Conversiestoornis [Conversion disorder]. *Huisarts Wet* 2011;54(10):560-4.
- Bischoff EW**, Boer LM, Molema J, Akkermans R, van Weel C, Vercoulen JH, Schermer TR. Validity of an automated telephonic system to assess COPD exacerbation rates. *Eur Respir J* 2012;39:1090-6.
- Sheikh A, Nurmatov U, Venderbosch I, **Bischoff E**. Oral immunotherapy for the treatment of peanut allergy: systematic review of six case series studies. *Prim Care Respir J* 2012;21(1):41-9.
- Bischoff EW**, Bourbeau J. Do COPD self-management programmes work? It is time to change our focus! *BMJ* 22 March 2012, *E-letter*. Available at: <http://www.bmj.com/content/344/bmj.e1060/rr/575073>.
- Uijen AA, **Bischoff EW**, Schellevis FG, Bor HH, van den Bosch WJ, Schers HJ. Continuity in different care modes and its relationship to quality of life: a randomised controlled trial in patients with COPD. *Br J Gen Pract* 2012;62(599):422-8.
- Bischoff EW**. Iedereen met COPD een exacerbatie-actieplan? [Does every COPD patient need an exacerbation action plan?] *Spreekuur Longziekten* 2012; 3(4).
- Uijen A, **Bischoff E**, Schellevis F, Bor H, van den Bosch W, Schers H. Continuïteit van COPD-zorg: effect van POH's en zelfmanagement [Continuity of COPD care: effects of practice nurses and self-management]. *Huisarts Wet* 2012;55(10):440-443.
- Bischoff EW**, Akkermans R, Bourbeau J, Van Weel C, Vercoulen JH, Schermer TR. Comprehensive self-management and routine monitoring in COPD patients in general practice: randomised controlled trial. *BMJ* 2012;345:e7642.
- Vercoulen JH, **Bischoff EW**, Heijdra YF. Werken met de Zorgstandaard COPD. Het 'Nijmegen Clinical Screening Instrument' als hulpmiddel [Working with the Dutch Standard of Care for COPD: using the 'Nijmegen Clinical Screening Instrument' as an aid]. *Ned Tijdschr Geneesk*, in press.

